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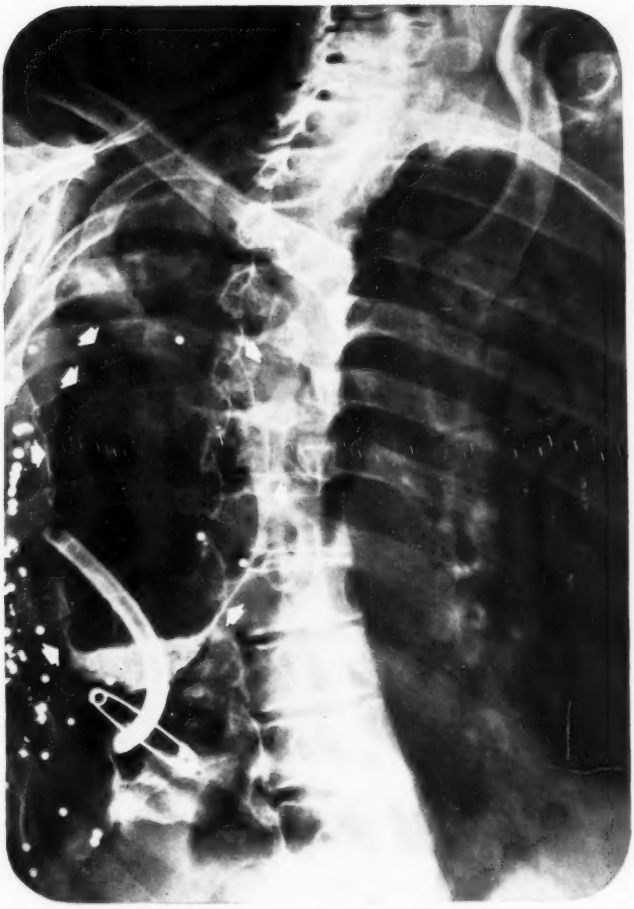

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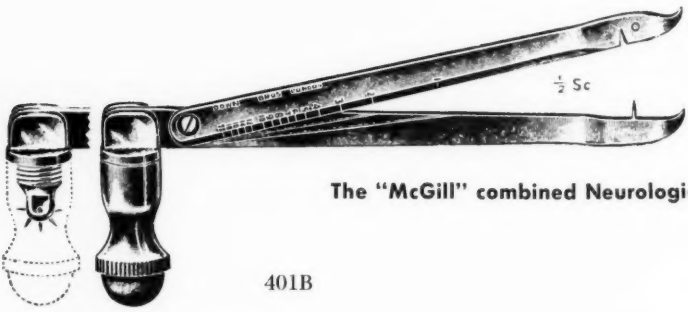

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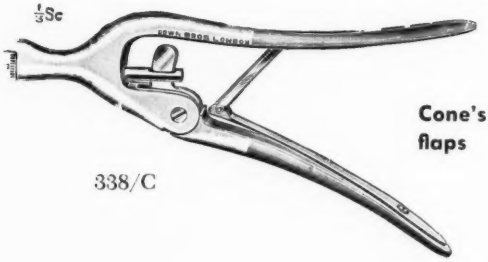

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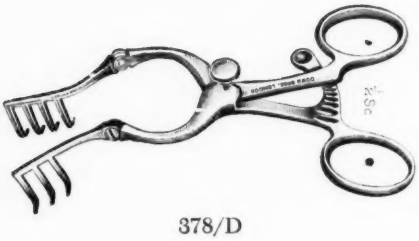

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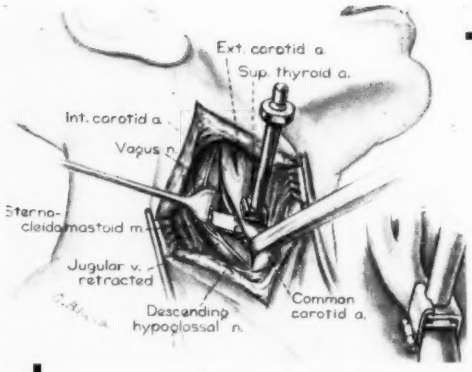

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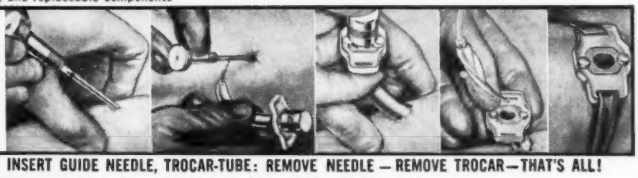

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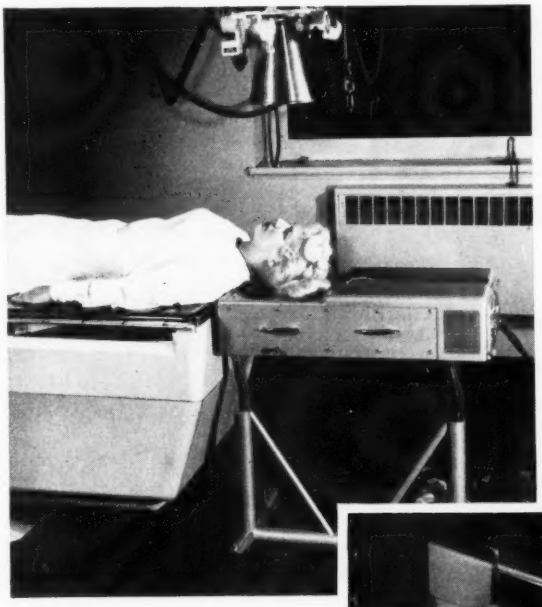

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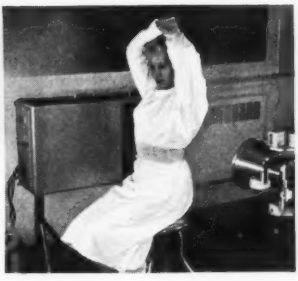

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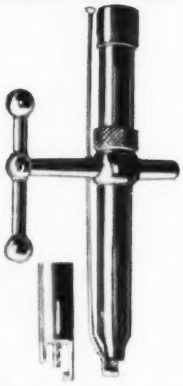

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Roanoke, Virginia

(Received for publication May 11, 1956)

EPIDURAL or peridural anesthesia is a form of regional block which has many advantages over general or spinal anesthesia. This type of anesthesia has been used effectively and enthusiastically by many individuals.[6–9,11,12,14] Its use in neurosurgery has been limited, and for this reason, the author wishes to report 125 consecutive cases of lumbar spine exploration under epidural anesthesia for excision of the intervertebral disc.

In the past few years, the introduction of more potent and longer lasting local anesthetic agents has made the use of epidural anesthesia in surgery more practical.[1,4,10,15] The drugs that have been used most frequently are lidocaine (Xylocaine) and hexylcaine (Cyclaine). In the majority of the cases in this report, the operations were done with 2 per cent lidocaine, although in a few 1 per cent hexylcaine was used. Both have given excellent anesthesia, but the series is too small to be of comparative value. Ansbro and associates[2] reported on the comparative use of these two drugs for epidural anesthesia in 2,000 cases of abdominal surgery. They preferred hexylcaine because of its lower incidence of toxicity. Crawford[5] also reported that Xylocaine and Cyclaine possess a high degree of potency and a short latent period with prolonged action, but when used in smaller concentration and volume, the incidence of toxicity was low.

TECHNIC

The patient is placed on the operating table in the prone position, and the table is adjusted to flex the spine. After the skin is prepared with an antiseptic agent, a #16 Tuohy needle is passed into the epidural space under local anesthesia at the 3rd or 4th lumbar interspace (usually the space above the suspected level of disc herniation). When the large needle meets the ligamentum flavum, one can usually feel a resistance, and when it is thrust through the ligamentum, there is a characteristic feel to its penetration. Once the needle is in the epidural space, fluid will flow into the space with ease, whereas force is necessary to infiltrate fluid into the tissues down to the ligamentum flavum. A drop of fluid in the hub of the needle, or in a glass adaptor attached to the needle, will reflect the presence of a negative pressure in the epidural space and will show a rise and fall with inspiration and expiration. If the intrathecal space is entered, there will be a free flow of spinal fluid from the needle. When this occurs, the needle should be withdrawn and introduced at

* Read at the meeting of the Harvey Cushing Society, Honolulu, Hawaii, April 16, 1956.

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the space below. This was necessary in only 2 instances. Also, if a patient has had a spinal tap for routine study or myelogram in the past 24 hours, one should avoid giving the anesthesia at the level of the tap.

Once the needle is in the epidural space, about 1 cc. (20 mg.) of the anesthetic agent is injected without force. If in a few minutes no signs of spinal anesthesia have developed, the remainder of the anesthetic agent is injected slowly and the needle is withdrawn. The usual dosage used in this series was 20 cc. of 2 per cent lidocaine (400 mg.). The head of the table is elevated so that the fluid will gravitate caudally. The skin along the line of the anticipated surgical incision is then infiltrated with 1 per cent procaine containing adrenalin, and the table is leveled. Since the skin is slow to become anesthetized, drapes should not be clamped to the skin unless it is first infiltrated with procaine. The subcutaneous tissues are usually well anesthetized from the epidural anesthetic in a matter of 10 minutes. Occasionally the anesthesia is supplemented with an intravenous drip of Demerol, Nembutal or Sodium Pentothal. There are occasions when the patient will have a very large midline disc herniation blocking the caudal flow of the anesthetic agent, or one exerting marked pressure on the nerve root, preventing diffusion of the agent about the nerve. In such cases, the patient may complain of pain when the root is retracted to expose the herniation. A few drops of 1 per cent procaine injected directly into the nerve with a very fine needle will make anesthesia complete.

ANALYSIS OF 125 CASES

There were no deaths and no convulsive reactions. Seventeen patients (13.6 per cent) had a drop in blood pressure that required a vasopressor drug. Eighteen (14.4 per cent) had pain on root retraction or on removing the cartilage. The pain was relieved in 10 cases by injecting the nerve with procaine, and in the other 8 by giving a small amount of Sodium Pentothal intravenously.

ADVANTAGES

The patient can be positioned for the epidural injection and operation at the same time. He is able to assume a comfortable posture under his own power, and the possibility of brachial plexus or peripheral nerve injury is reduced. Having the patient awake in the prone position obviates the necessity of an endotracheal tube. The single injection technic of lumbar epidural anesthesia is relatively simple, and when supplemented with local infiltration of the skin, permits one to start the operation without delay. The advantages of doing an operation under local anesthesia bear emphasis. In recent years much stress had been placed upon the prevention of cardiac arrest, and even though cardiac arrest has sometimes been attributed to epidural anesthesia, the cause remains the same—namely, diminished oxygen tension. The author feels that this potential danger is less with epidural than with general anesthesia. Certain patients of poor physical status can be operated upon more safely under epidural anesthesia, particularly those with cardiac or pulmonary disease. In this series are 2 patients with previous coronary occlusion who showed no untoward effects from epidural anesthesia. In those patients with pulmonary disease in whom alveolar diffusion of oxygen is impaired, as with emphysema, bronchiectasis, asthma, and even in heavy smokers, epidural offers a definite advantage over general anes-

thesia. Another very distinct advantage of epidural anesthesia, in my experience, is that less bleeding occurs than with general anesthesia. Muscle relaxation is consistently better. Other advantages over general anesthesia are virtual absence of postoperative nausea and vomiting, and less chance of atelectasis and pneumonia. Finally, the hazard of explosion is nil.

The advantages of epidural over spinal anesthesia are: (1) The danger of neurological sequelae which occasionally occur with spinal anesthesia, such as reported by Bergner and associates,[3] is minimal. (2) There is no possibility of extension of the anesthetic agent intracranially, and the anesthesia can be carried into the cervical region without affecting respiration. (3) There is no post-anesthesia headache. (4) There is no temporary paraplegia. (5) There is no postoperative urinary retention. (6) A drop in blood pressure, when it occurs, is seldom profound or precipitous.

DISADVANTAGES OF EPIDURAL ANESTHESIA

A large dose of anesthetic agent is necessary for epidural anesthesia (400 mg. as compared with 20 mg. required for spinal anesthesia), and if injected intrathecally may prove disastrous. Complications can be avoided by first injecting 1 cc. (20 mg.) and waiting several minutes for any sign of spinal anesthesia before giving the full dose. It is a procedure that requires an experienced technician to administer, but one quite adaptable for the neurosurgeon. In this series of 125 cases, no intrathecal administration was encountered. Another disadvantage is the possibility of toxic reaction to the anesthetic agent. Ansbro *et al.*[2] reported 11 instances of convulsive reactions in 1,000 cases of epidural anesthesia in which 2 per cent lidocaine was used (1.1 per cent incidence) and 1 reaction in an equal number of cases in which 2 per cent hexylcaine was the anesthetic agent (0.1 per cent incidence). In this report, there were no convulsive seizures or other severe toxic reactions to either drug. Intravenous fluids should be running, and oxygen should be available for positive pressure administration. Occasionally there is a fall in blood pressure, but this is associated more frequently with rapid injection of the anesthetic agent. The amount of adrenalin used in the procaine for skin infiltration may help counteract this drop in pressure. If not, methoxamine (Vasoxyl) or phenylephrine (Neosynephrine) intramuscularly will promptly restore the blood pressure to normal. It is felt that a moderate drop in blood pressure is a less serious complication than a marked rise. Fear of local anesthesia by the patient can be a disadvantage, but with adequate premedication or light Sodium Pentothal anesthesia, the patient seldom questions the operator as to what is being done. A case of aseptic meningitis following epidural anesthesia was reported by Jenicek.[13]

SUMMARY

Epidural anesthesia is very satisfactory for excision of the lumbar intervertebral disc and has distinct advantages over general or spinal anesthesia. It was used in 125 consecutive cases without mortality or serious complications.

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THE ROLE OF PERINEURIAL SACRAL CYSTS IN THE SCIATIC AND SACROCOCCYGEAL SYNDROMES

A REVIEW OF THE LITERATURE AND REPORT OF 9 CASES*

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PERINEURIAL sacral cysts as a cause of low backache, sciatic and sacrococcygeal pain, and of sensory and motor deficits were described by Tarlov,[14–17] and further confirmation has come from other reports.[1–6,8–10,12,13,20]† In reviewing 28 reported cases it was noted that backache and sciatic pain were present in about two-thirds of the group, while motor and sensory deficits of sacral nerve function were present in about one-fourth of the series. In a few instances, other pathologic conditions were found, which if present alone, might have caused the sciatic and sacrococcygeal syndromes. In the writers' brief and limited experience with 9 patients who have had intrasacral cysts the question has arisen in 5 cases as to whether or not these cysts were necessarily the cause of the sciatic syndrome. It seems of more than ordinary interest, then, to review each of these cases as to the rôle played by the perineurial sacral cyst in causing the sciatic and sacrococcygeal syndromes, and to inquire in a similar manner into the cases reported in the literature.

REVIEW OF PERSONAL CASES

Perineurial Sacral Cysts—? Symptomatic

Case 1. The first real question concerning the validity of the assumption that these cysts are the cause of the syndrome came when a fairly large perineurial sacral cyst was incidentally discovered when exploring a sacral canal for an unexplained low backache, pain in the buttocks and perineum, and sciatica of 4 months' duration in a 58-year-old housewife. The cyst was not disturbed, for on further search the major lesion proved to be a large abscess in the body of the sacrum, extending well anterior to it. The wall of the abscess was biopsied but no tumor was found. The abscess cavity was drained, with subsequent relief from pain (Fig. 1). Somewhat later the sacral abscess proved to be one of several malignant metastatic lesions.

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† There may be some justifiable doubt as to the accuracy of including such reports as those of Archer *et al.*,[2] Baker and Webb,[3] and Schurr,[9] since in these cases the intrasacral lesion may have been an entirely different type of cyst (meningocele or arachnoidal diverticulum). Such may be the situation in our Case 9. However, for practical clinical purposes, they may be grouped together, though it is indeed well to recognize their differences, both etiologically and histologically.

FIG. 1. *Case 1.* Lateral view of sacrum, disclosing residual Pantopaque and erosion of the vertebral bodies. Catheter is *in situ* in abscess cavity. The perineurial sacral cyst did not fill with Pantopaque.

Case 2. In another patient, a 38-year-old railway worker with a sciatic syndrome, a myelogram disclosed the presence of both a herniated intervertebral disc (L4, left) and a left S2 perineurial sacral cyst (Fig. 2). Imbrication of the cyst wall, after removing a part of it, and removal of the protruded disc, gave only temporary relief. In the immediate postoperative period there was marked sensory loss over the left side of the saddle area, with mild weakness of urinary and rectal sphincters. He improved for a while under prednisone (Meticorten) therapy, only to have recurrence of severe sciatic pain.

At re-exploration more disc material had prolapsed, at the L4 level, and another protrusion was present at the L3 level, causing severe compression of the cauda equina. The disc spaces were thoroughly curetted, and a dowel interbody type of fusion was performed at L4–5. He made a slow recovery with considerable but not complete relief from pain. Sensation returned to the genitals and perineum, and control of rectal and urinary sphincters returned to near normal status. More recently pain has increased; if this persists, a high thoracic anterolateral cordotomy may be indicated.

Case 3. A third case also has cast some doubt as to the rôle played by these perineurial sacral cysts in the sciatic syndrome. This patient was a 58-year-old lady who was seen on July 8, 1955, with complaints of low-back, left groin and *left* sciatic pain which began in February, 1955. In addition to the usual signs of an acute low-back syndrome, the Lasègue sign was negative, and percussion over the sacrum elicited distress in the lower back and left posterior thigh. A Pantopaque myelogram (Fig. 3) disclosed bilateral perineurial sacral cysts, the one on the left being larger. On surgical exploration it measured 3.5×2.5×3 cm. in its greatest diameters, and appeared to involve the left S2 and S3 roots. Sections of the cyst wall, stained by hematoxylin and eosin, Mallory's trichrome, and Bodian stains, disclosed myelinated nerve fibers coursing through the fibrous tissue of the cyst wall (Fig. 4).

She obtained very little relief from this surgical intervention and began to experience *bilateral sciatic pain* and low backache. We chose to re-explore the wound and to look for cysts on the right side and disc protrusions. A transverse posterior protrusion of the lumbosacral disc was encountered and removed. Perineurial sacral cysts on the *right* S2 and S3 roots were subtotally removed and the sheath of the nerve root was reconstructed. She has had 80 per cent relief from pain, with minimal residual sensory loss over the S2, 3 and 4 dermatomes.

Case 4. Another example of the presence of a herniated disc with intrasacral cysts may be recorded to emphasize this point and that these cysts may be multiple.

FIG. 2. *Case 2.* Myelogram with Pantopaque filling large left perineurial sacral cyst. Defect between this cyst and column of contrast medium proved to be caused by protruded disc.

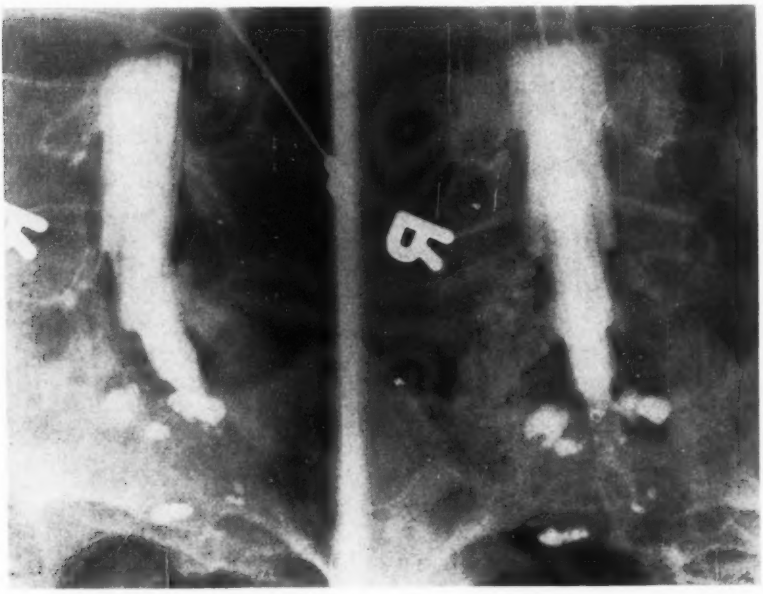

FIG. 3. *Case 3.* Oblique and anteroposterior views showing minimal amount of Pantopaque in multiple perineurial sacral cysts.

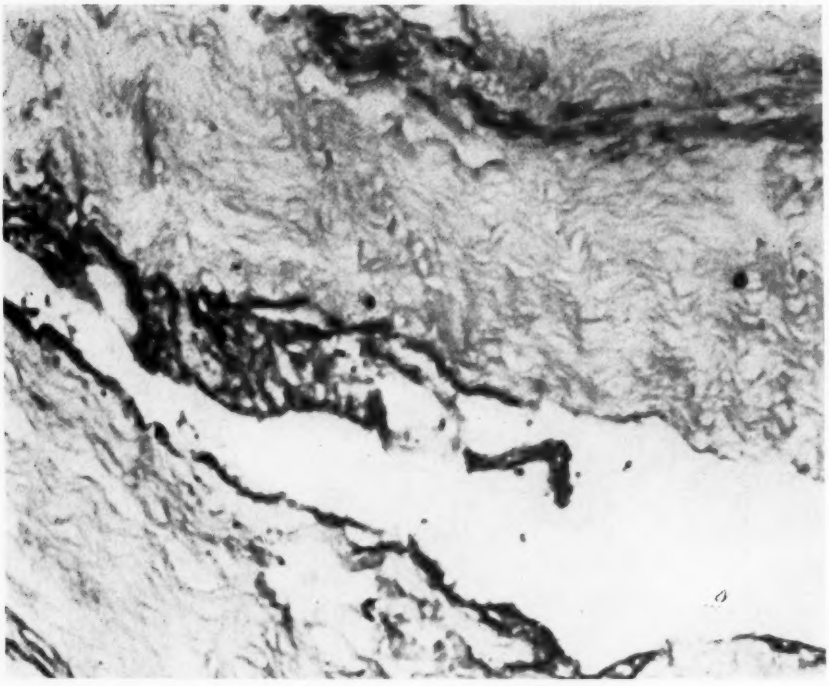

FIG. 4. *Case* 3. Photomicrograph of wall of perineurial sacral cyst, suggesting the presence of myelinated nerve fibers in a fairly dense fibrous-tissue structure. (Mallory trichromic stain, ×175)

A 43-year-old female, seen on March 14, 1956, had experienced the sudden onset of pain in the lower back, left hip, posterior thigh and leg, while at lunch 8 weeks previously. Some weakness of the leg was noted. The pain persisted. The neurologic findings were normal. A myelogram (Fig. 5), performed elsewhere, disclosed bilateral multiple small grape-like collections of Pantopaque in the sacral canal, but there was no evidence of lumbar disc herniation. A discogram gave evidence of a degenerated "bulging" lumbosacral disc. This was confirmed at exploration (March 26, 1956). At the same time a grape-sized (8×12 mm.) cyst was seen on the left 1st sacral root. This was exposed and its contents were seen to communicate with the subarachnoid cyst. It was not removed. The patient has done well postoperatively with relief from pain.

Case 5. In this case the findings and course may be somewhat less convincing. A 67-year-old carpenter, seen in March, 1955, had experienced left sciatic pain since an injury the previous November. While lifting a board on a trestle, one end slipped and he felt a snapping in the lower back as his back acutely flexed. Pain appeared immediately in the posterior aspect of the left lower extremity and was accompanied by numbness of the sole of the left foot. Cough, sneeze and strain aggravated the discomfort. Some improvement in symptoms occurred before the pain became more severe. A perineurial cyst was demonstrated by Pantopaque myelography on the right 1st sacral root (Fig. 6). Immediately after myelography his pain disappeared, and as long as a year later it has not returned.

FIG. 5. *Case 4.* Residual Pantopaque in small grape-like perineurial sacral cysts noted at time of discography and confirmed at surgery.

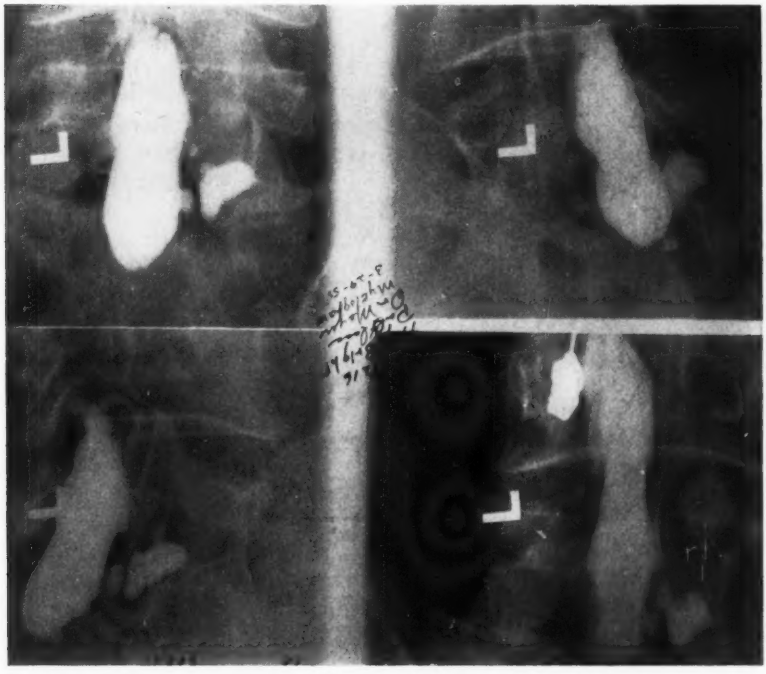

FIG. 6. *Case 5.* Multiple views of perineurial sacral cyst (right S1).

Comment. Certainly a case such as Case 5 is inconclusive, since one may assume either a positive or a negative attitude towards the possibility that the cyst caused the patient's pain. But assuming that it did cause his pain, then it is apparent that these lesions, like intraspinal tumors and herniated intervertebral discs, may be asymptomatic at times and, for no apparent reason, may become symptomatic. Similar reports have been recorded in the histories of other cases of sacral canal cysts. It is evident, then, that symptoms may be intermittent.

REVIEW OF REPORTED CASES

Perineurial Sacral Cysts—? Symptomatic

A search for other asymptomatic sacral cysts and for those cysts that were associated with other lesions capable of producing similar symptoms brings out a few excellent examples.

1. In the report of Taheri *et al.*[13] there was noted a "bulging of the [lumbosacral] disc in the region of the posterior ganglion of the right 1st sacral nerve." A perineurial sacral cyst, measuring 5×7×3 mm., with its associated 2nd sacral root was excised between clips. A smaller cyst (3×3×5 mm.) on the left 2nd sacral root apparently was asymptomatic and was not removed. The low backache and right sciatic pain were relieved.

Comment. One might well question as to just which pathologic condition, the bulging disc or the sacral cyst, was causing the symptoms on the right side. Certainly from the report one must conclude that the left 2nd sacral cyst, which was nearly as large, was asymptomatic.

2. Another report of a lumbar disc protrusion in association with an intrasacral cyst occurred in 1 of 2 cases of perineurial sacral cysts reported by Strully and Heiser.[12] After removal of a herniated lumbosacral disc, an incidental intrasacral cyst was discovered under the lamina of S1. The cyst was uncovered (decompressed?) by sacral laminectomy, but it was not excised. The patient recovered free from pain. They remarked that an "intrasacral cyst may be asymptomatic."

3. Another case in which there appeared a lumbar disc herniation and perineurial sacral cyst on the same side with the presenting symptom of pain was reported by Jacobs *et al.*[5] This patient, 5 years previously, had undergone a laminectomy for severe sciatic pain, and a hypertrophic ligamentum flavum was removed. He was re-explored in the following year, and remained free of pain until he injured himself again in 1953. A myelogram disclosed a small herniated lumbosacral disc and a perineurial sacral cyst, 1 cm. in diameter, on the 2nd and 3rd sacral roots, both on the side of the pain. The herniated disc and the perineurial sacral cyst were both resected, with relief from pain. They commented that the disc may have accounted in full for the symptoms but the perineurial sacral cyst could have caused them.

4. In Tarlov's fifth and most recent case, the patient had a herniated lumbosacral intervertebral disc and a cyst on the 2nd sacral root, as well.[19]

5. Seaman and Furlow[10] noted that "the clinical significance of these cysts is difficult to evaluate." Even though in most of the cases reviewed the cysts have been associated with sciatic pain, 2 of their 4 patients with sacral cysts "were asymptomatic and the cyst was an incidental finding."* They further stated, "It may be that cysts that do not communicate with the subarachnoid space are more likely to cause symptoms and as the fluid accumulates they enlarge, become tense, and press on adjacent nerves. On the other hand, one of the largest cysts in our series which did not communicate with the subarachnoid space occurred in an asymptomatic patient."

From our experience it is apparent that symptomatically it makes no difference whether or not the cyst communicates with the subarachnoid space, for either type of cyst may or may not cause symptoms.

6. It will be recalled that Rexed's[7] description of perineurial cysts was from autopsy material in which "all the persons from whom material for this study was taken were affected by lateral disc protrusions." He was of the opinion that "There is a possibility that the cystic formations can be traced back to some developmental disturbance, but so far nothing has been brought forward that supports such a theory." Detailed clinical records were not available to him, but he concluded: "Naturally the development of arachnoidal proliferations of the severity seen in some of the cases must give symptoms from the affected roots." He further suggested that such a nerve should be more vulnerable to any type of irritative phenomena, such as trauma or infection. In Rexed's report, therefore, the rôle played by the cysts or the protruded discs in producing symptoms was impossible to determine.

A glance at the myelograms in the cases reported previously and in those presented here will disclose frequent examples of multiple bilateral sacral cysts (usually "cranberry- to grape-size") in which the symptoms were noted to be unilateral. Sometimes, but not always, these occurred on the side of the largest cyst. Unilateral symptoms when equally large cysts were present bilaterally occurred in our Case 3; however, after surgical interference on one side, the contralateral side became symptomatic. Whether or not this was caused by the transverse posterior protrusions of the lumbosacral disc or to postoperative changes in the contralateral perineurial sacral cyst remains unsolved, since both pathologic structures were treated surgically.

PERSONAL CASES

Perineurial Sacral Cysts, Symptomatic, and Without Other Intraspinal Lesion

For undoubted proof that perineurial sacral cysts may and do produce symptoms, they should occur unassociated with other intra- or extraspinal lesions capable of producing the sciatic and sacrococcygeal syndromes.

* In 1 case a cyst was tapped upon attempting caudal anesthesia for hemorrhoidectomy. In another case a sacral cyst was an incidental finding on performing cervical myelography.

The remaining reported cases do seem to substantiate Tarlov's[15] original thesis.

In addition to these, we have studied 3 patients who had symptomatic perineurial sacral cysts without other recognizable intra- or extraspinal pathologic conditions that might produce pain, or sensory or motor disturbances. Since these cases further emphasize the rôle that perineurial sacral cysts can play in the sciatic and sacrococcygeal syndromes, they are recorded here in detail. A fourth patient's (Case 9) intrasacral cyst is of questionable etiology and character. It may have been an intrasacral meningocele or arachnoidal diverticulum. However, its appearance and the signs and symptoms so closely simulate those of a perineurial sacral cyst that it is recorded.

Case 6. A 49-year-old male had experienced some low backache off and on for 1½ years after *wrenching* his back when he fell through a trap door and landed on his right hip. Eight years previously he had strained his back while lifting a 300-pound pan of metal plates—a short man on the other side had dropped his side of the pan. Six months before hospitalization, typical left lower backache began, accompanied by left sciatic pain that spiraled down to the medial aspect of the knee. Dental extractions and osteopathy were of no help. Two months prior to admission, bilateral hip and sciatic pain became more severe and was aggravated by sitting, coughing, sneezing, and the act of arising from bed. He obtained some relief from the use of a hard bed and from walking about.

Examination disclosed marked splinting of the muscles of the back, with severe limitation of motion of the spine and with a list to the left. Both knee and ankle jerks were absent. Hyperalgesia was present over the right S1 dermatome, and slight hypalgesia was noted in areas over the left S1, 2 and 3 dermatomes. The spinal fluid contained 30 mg. per cent protein. The myelogram (Figs. 7 and 8) disclosed bilateral sacculation of the Pantopaque in the S1 and 2 roots, consistent with that seen in perineurial sacral cysts.

At surgery, July 12, 1949, typical thin-walled translucent cysts with nerve fibers in their walls were found on S1 and S2 roots, as well as smaller cysts on the S3 roots. These were treated by incision and then imbrication with No. 5-0 silk sutures, and covered with Gelfoam. Inasmuch as there were degenerative changes of the lumbosacral disc, a Hibbs type of fusion was done.

The patient has made a complete recovery. He is able to do heavy work and rarely has any discomfort. He was last seen in March, 1956.

Case 7. A 53-year-old female was seen March 5, 1954, because of incontinence of urine, weakness of the lower extremities (the left worse than the right), tingling paresthesia in the left lower extremity and a dull ache in the lower back and buttocks. All symptoms began following an injury to her back on January 8, 1953. There had been only mild progression of her symptoms after they had become well established.

Examination revealed a left Horner syndrome, markedly reduced ankle jerks and an unsteady gait, apparently caused by weakness of the pelvic girdle. There was mild hypesthesia over the perineum and buttocks, with moderate weakness of both urinary and rectal sphincters. Percussion over the upper sacral and the lower lumbar spines elicited distress. Plain roentgenograms of the sacrum disclosed a

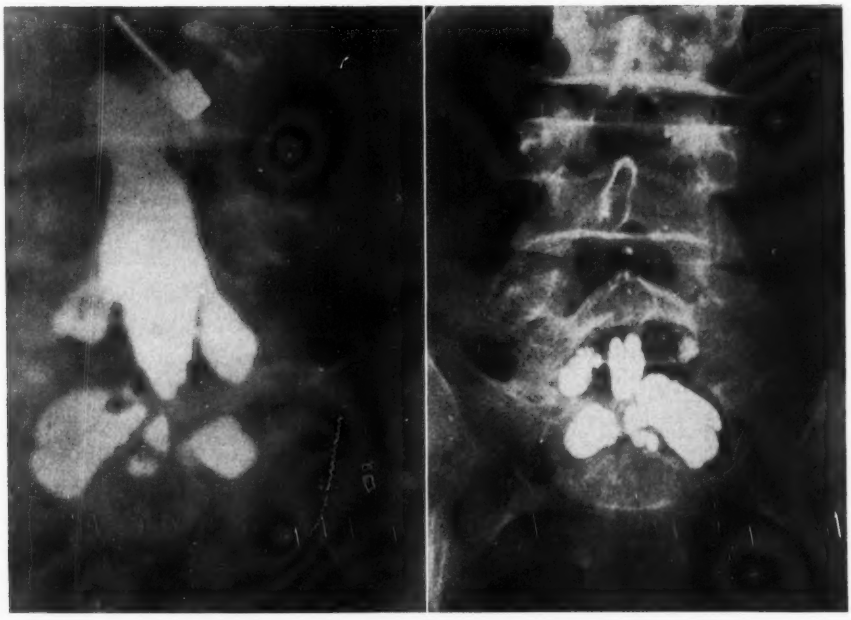

FIG. 7. *Case 6.* (Left) Pantopaque myelogram (anteroposterior view), in the erect position, showing partial filling of multiple perineurial sacral cysts. (*Right*) Same view in horizontal position after removal of Pantopaque, showing residual opaque medium in the cysts.

FIG. 8. *Case 6.* Oblique view (same myelogram as in Fig. 7), suggesting enlargement of sacral canal.

FIG. 9. *Case 7.* (*Left*) Multiple perineurial cysts partially outlined by Pantopaque as seen in anteroposterior view. (*Right*) Oblique view.

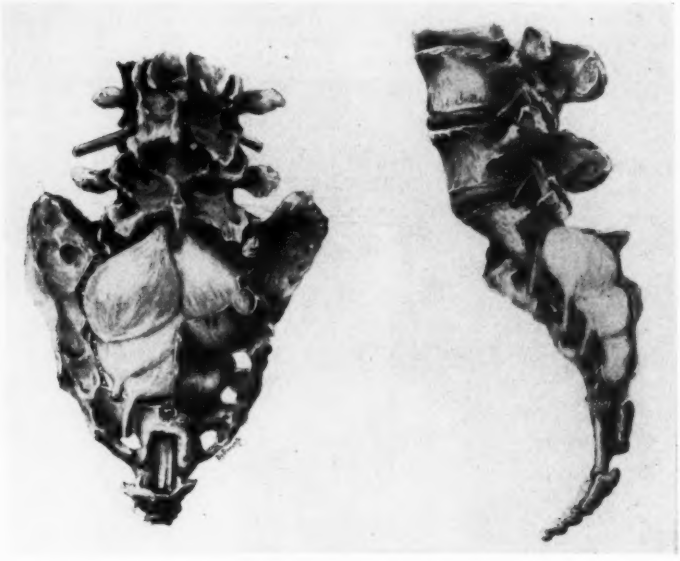

FIG. 10. *Case 7.* Artist's conception of the multiple perineurial sacral cysts, emphasizing the erosion and ballooning of the sacrum.

markedly enlarged, scalloped sacral canal. A Pantopaque myelogram (Fig. 9) disclosed rather large arachnoidal cystic defects on S1 and S2 roots and to a lesser degree on others.

At surgery, April 15, 1954, the left side of the paper-thin posterior arch of the sacrum was opened, revealing large cysts on S1, S2 and S3 roots with nerve filaments coursing through the walls of these cysts (Fig. 10). With only minor tech-

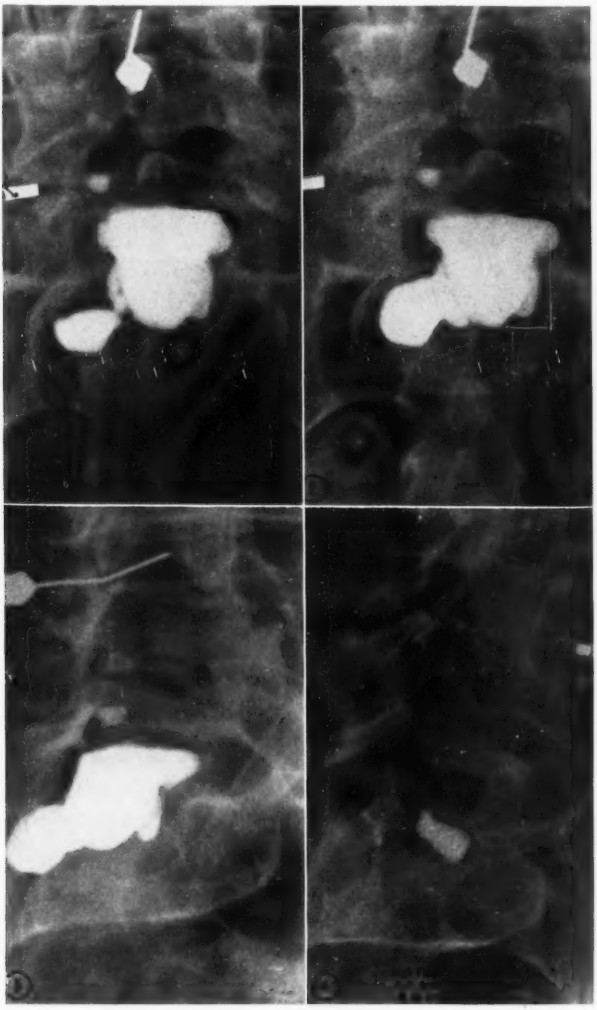

FIG. 11. *Case 8.* (1, 2, 3) Multiple views of a Pantopaque myelogram disclosing a perineurial cyst on the right 1st sacral root. A droplet of contrast medium appears loculated at the L4-5 level, suggesting a possible small arachnoidal pouch. (4) Oblique view taken after removal of the Pantopaque, showing residual opaque medium in the cyst.

nical difficulties caused by epidural venous hemorrhage, the cysts were handled easily by means of imbrication with No. 5-0 silk sutures and by covering them with Gelfoam.

The postoperative course was not unusual, but the patient has been left with considerable sensory deficit in S2 and S3 dermatomes, and with slightly increased sphincter weakness. The pain on the left side has been markedly relieved, but on the right (unoperated) side hypesthesia of buttocks and perineum, and sciatic pain have appeared.

Case 8. A 76-year-old white male was admitted to the hospital July 7, 1954, because of 5 weeks of right sciatic pain. Some months before this he may have wrenched

FIG. 12. *Case 9.* Roentgenogram of sacrum revealing huge dilatation of sacral canal.

his back. Soon after the pain commenced he noticed a right footdrop. The ipsilateral knee and ankle jerks were absent. A myelogram (Fig. 11) revealed a small perineurial sacral cyst at the S1 level on the right side.

At surgery a small perineurial cyst, about 1 cm. in diameter, was found and subtotally removed. The rest of the wall was imbricated with No. 5-0 silk. The posterior root ganglia of S2 and 3 were found to be larger than normal and appeared to be inflamed. He made a rapid and complete recovery and has returned to his former occupation as a wholesale hardware salesman.

Case 9. On June 20, 1954, a 28-year-old white female was admitted to the service of Dr. H. E. LeFever at the University Hospital. She had experienced urinary and rectal incontinence since childhood, and weakness of her lower extremities since she was 16 years of age.

On examination it was found that the deep tendon reflexes in the lower extremities were absent, with hypesthesia and hypalgesia in the sacral dermatomes—more severe on the left side. A high steppage gait prevented her from climbing stairs without the aid of her hands to pull herself up by a handrail. There was considerable atrophy of the muscles in the lower extremities and the buttocks.

Roentgenograms of the sacrum revealed a very large sacral canal with obvious thinning of the posterior bony plate (Fig. 12). A myelogram (Fig. 13) disclosed

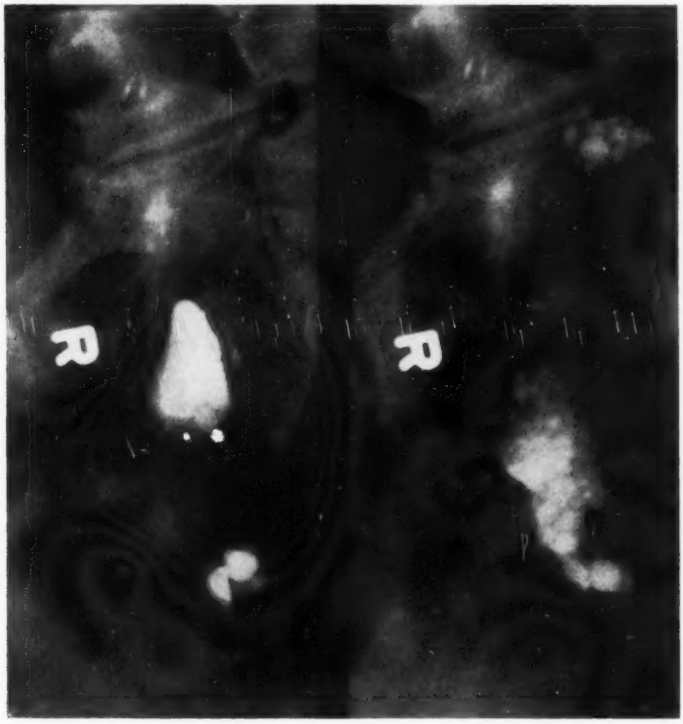

FIG. 13. *Case 9.* Myelogram, anteroposterior and oblique views, with Pantopaque present in the large sacral canal cyst.

evidence of a large cyst that occupied the sacral canal. There was a small opening between the cyst and the cul-de-sac of the normal lumbosacral leptomeninges.

The operation performed by Dr. LeFever was reported as follows: "The spine and the lamina of L5 were removed, as well as the thin layer of bone overlying the sacral hiatus. It was immediately apparent that a large sacral cyst was present, arising from the inferior portion of the cul-de-sac. The whole cyst was resected free, and this occupied the left side of the dural sac and extended inferior to the cul-de-sac. The opening was at the extreme end of the cul-de-sac. The whole cyst was removed, and the dura was opened in order to be certain that this represented the only opening. The filum terminale was sectioned, and the dura was repaired. The

cyst extended from the 1st to the 4th sacral segments, greatly enlarging the sacral canal."

The patient now walks with only slight impairment in her gait, and has no sphincter weakness or incontinence and no pain or distress. She has returned to work at full time.

Sections of the cyst have failed to disclose any nerve fibers in its structure (Fig. 14). For this reason, and because of its gross appearance, it may be that it is an intrasacral meningocele or intrasacral arachnoidal herniation or diverticulum.

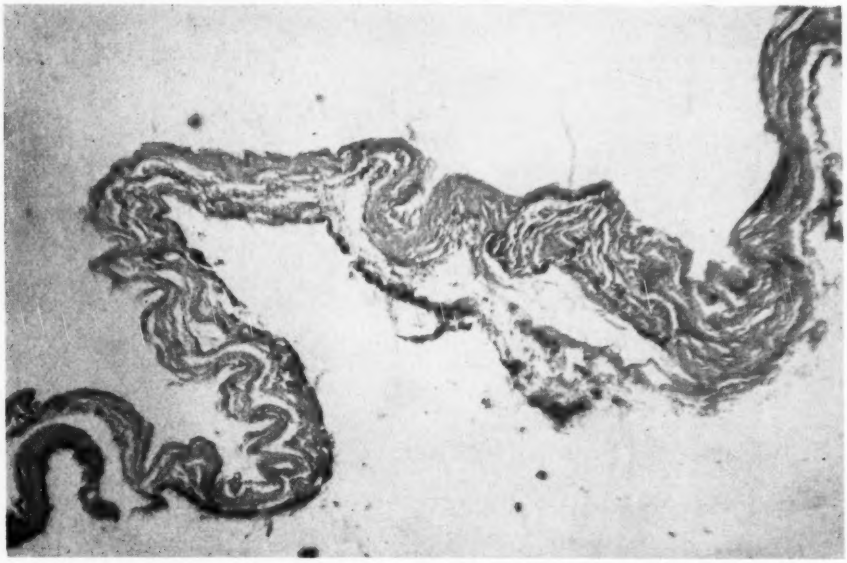

FIG. 14. *Case 9.* Photomicrograph of cyst wall, which appears to be made up of fibrous and collagenous tissue with some areas of "pavement" type cells on its inner surface. No nerve fibers were found. (Hematoxylin and eosin, ×175)

DISCUSSION

At least 3 of the above 4 cases, together with the remaining cases reported in the literature, seem to establish beyond much doubt that perineurial sacral cysts may produce symptoms.* The reasons why they produce symptoms are not always easy to understand, and just as unclear may be the reason why another cyst of similar size and location in the same patient or in others does not produce pain or other symptoms. An analogous situation is encountered not infrequently with disc protrusions and, less

* An analysis of the symptoms in 17 clinical cases collected by Tarlov[19] and presented before the Johns Hopkins Surgical and Medical Association in February, 1955 showed the following: sciatic syndrome alone, 11 patients; sciatic syndrome with caudal sacral syndrome (disturbed perineal sensation and urinary retention or incontinence), 3 patients; urinary disturbance alone, 1 patient; low-back pain radiating to the front of the thigh, 1 patient, in whom the cyst arose from the 1st lumbar nerve root and produced a complete spinal block; and sacral coccygeal and rectal pain, 1 patient.

commonly, with intraspinal tumors (neurofibromas). Of further interest, and unexplained, is the presence of unilateral symptoms when bilateral cysts are present (bilateral cysts were present in Cases 3, 4, 6 and 7, but initial unilateral symptoms occurred in Cases 3 and 4). What spontaneously initiates pain impulses in "delta" fibers is still an interesting chapter in peripheral nerve and spinothalamic physiology.

The etiology of perineurial sacral cysts may give some clue as to why they may produce symptoms. Tarlov[18] put forth convincing evidence for the traumatic origin of these cysts; blood may invade the nerve root between the endoneurium (derived from the pia mater) and the perineurium (derived from the arachnoid), with resultant distention of the space (perineurial). The cyst thus forming becomes surrounded by compressed nerve fibers. Extensive degenerative changes in the neural elements in the cyst were found in many instances, a fact we have confirmed in biopsies from the cyst walls. From this evidence one may assume logically that such changes could produce neural dysfunction of the order seen clinically.

If unusual pressure factors within the sacral canal can produce symptoms (as pressure applied elsewhere to nerve fibers may do) then the scalloped enlargement of the sacral canal, as shown by roentgen ray and surgical exploration, confirms that such pressure is present. This same pressure is also applied to the nerve fibers as they are stretched out in the cyst walls. Similarly, the pressure of the distended cyst is applied against contiguous sacral roots, not unlike any other intraspinal mass, and may be sufficient cause for the symptoms assigned to these cysts.

SUMMARY

It has been shown that a few sacral cysts, assumed to be perineurial sacral cysts, are incidental findings at autopsy, myelography, and needle and surgical exploration of the sacral canal; also they may be found associated with other spinal lesions (lumbar disc herniations and sacral abscess), capable in themselves of producing sciatic and sacrococcygeal syndromes. In the case of multiple intrasacral cysts, it is shown that they may all be asymptomatic, or unilateral symptoms may appear. It is likewise apparent that the symptoms may be intermittent, just as are the symptoms of other intraspinal mass lesions. Pressure distention of the affected nerve fibers, with degenerative changes, and pressure against contiguous nerve roots are emphasized as causative factors in producing the sciatic and sacrococcygeal syndromes.

To the reported cases of perineurial sacral cysts are added 3 cases of perineurial sacral cysts causing typical symptoms. In a fourth case (Case 9) the lesion may have been an intrasacral meningocele. It is believed that the etiologic rôle played by the perineurial sacral cyst in the sciatic and sacrococcygeal syndromes is now well established. This lesion is another of many that must be considered when patients present themselves with low-back or sciatic pain, or sensory or motor deficits of sacral root distribution.

Four other cases are briefly detailed in which perineurial sacral cysts were associated with other lesions (3 with disc herniations and 1 with a sacral abscess). In a fifth case, in which a perineurial sacral cyst was demonstrated radiologically, the symptoms disappeared after myelography.

ADDENDUM

Since this paper was submitted for publication, another report on the subject has appeared. Strully[11] described 4 additional cases and suggested the term "meningeal diverticula" as more appropriate, believing these are more truly arachnoidal diverticula of nerve roots and not necessarily degenerative cysts. Two of his patients had associated herniated discs. In his Case 2 an L4 disc protrusion had been removed some $3\frac{1}{2}$ years before, without complete relief from pain. After removal of the sacral root diverticulum "the patient had partial relief of pain." In Case 3, an L4 disc was associated with sacral diverticula and he remarked that "This patient's symptoms were due to the disk herniation exclusively." Strully seems to be of the opinion that the smaller cysts at this stage may not produce symptoms but as they enlarge and erode the bone (enlarge the sacral canal) they will cause pain. He further stated, "The cause of pain in these cases is obvious. Diverticula of nerve roots are well limited by the bony canal in which they lie. As the mass increases in size, the filaments of the sensory roots are stretched over the periphery of the lesion and compressed against the walls of the sacral canal. Adjacent roots are also compressed. The pressure must be great, since erosion of the sacrum also occurs. With further thinning of the dorsal sacral plate, the periosteum is involved and another source of pain added." Elsewhere one of us (KHA) has emphasized that many of these cysts communicate with the cerebrospinal fluid and frequently may be diagnosed by myelography. If a little contrast medium is left in the canal it is useful to make another x-ray film on the following day, for Pantopaque may by then have entered into one or more sacral cysts; these facts and the erosion of the sacrum with enlargement of the sacral canal are also emphasized by Strully.[11]

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ACETYLCHOLINE AND SEROTONIN IN THE SPINAL FLUID*

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THIS paper reports quantitative analyses of acetylcholine and serotonin in the spinal fluid of patients with head injuries, brain tumors, and other neurological disorders. It also reports the related findings in dogs subjected to experimental concussion of the brain.

Acetylcholine occurs in the spinal fluid of animals after experimental head injury. This, Bornstein[2] postulated, is released from the mechanically damaged brain cells, a supposition in keeping with Lorente de Nó's[8] work showing that acetylcholine is released from peripheral autonomic ganglia by mechanical damage only. Either because of excessive production of acetylcholine or impaired destruction, the acetylcholine, which never normally appears in the spinal fluid, occurs in significant amounts after trauma.

In 1950 Ward[11] proposed the use of huge doses of atropine in the treatment of closed head injuries to combat this release of acetylcholine. Since 1951 we have been using Ward's regimen in the treatment of selected severe head injuries. We feel that it may have helped some patients recover who otherwise might not have done so. A control series of patients treated without atropine is being run. We hope with a larger number of cases to ascertain whether there is a significant difference in the results. Recently Jenkner and Lechner,[7] reporting on 309 patients with severe head injuries, found that 249 of them, treated with anticholinergic drugs, got well quicker and had fewer complications. They also noted that the electroencephalograms in this group returned to normal faster than those in the group not receiving anticholinergic therapy.

It became evident from the first that a quantitative study of the amount of acetylcholine in the spinal fluid of these patients would be of value in order to determine the effectiveness of anticholinergic therapy. Ruge[10] has studied this in animals. The technique of acetylcholine determination is a tedious one, utilizing one of various methods of biological assay. The most sensitive technique makes use of the heart of *Venus mercenaria*, the common clam. This method was introduced by Welsh[12] and is very specific, but any significant amount of blood in the spinal fluid will immediately destroy the

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acetylcholine because of the cholinesterase in the red cells. Therefore, in studying patients with head injuries the traumatic subarachnoid hemorrhage so frequently present invalidates determinations of spinal fluid acetylcholine, but not of serotonin. Likewise, because of the notorious dangers of doing lumbar puncture in the presence of increased intracranial pressure, in many cases we did not take spinal fluid specimens from patients in the acute phase following injury.

Much interest has been manifested recently in the neurohormone, serotonin, chemically identified as 5-hydroxytryptamine.[9] This substance is identical with enteramine, isolated from the intestinal mucosa.[5] Hematologists have been interested in serotonin because of its rich occurrence in platelets and its vasoconstrictor effect. However, the discovery of serotonin in the brain[1] is an important landmark in neurology and psychiatry. The

TABLE 1

Neurochemical effects on the regularly contracting heart of the clam

Substance	With Sea Water	With LSD	With Mytolon
Acetylcholine	↓ Contraction	↓ Contraction	Normal contraction
	↓ Rate	↓ Rate	Normal rate
Serotonin	↑ Contraction	Normal contraction	↑ Contraction
	↑ Rate	Normal rate	↑ Rate
"X" Substance	↓ Contraction	↓ Contraction	↓ Contraction
	↑ Rate	↑ Rate	↑ Rate

hypothesis that serotonin has a role in brain function is supported by the fact that lysergic acid diethylamide (known as LSD), a powerful psychotogenic and hallucinogenic drug, is the most powerful imitator of serotonin *in vitro*. In addition, reserpine, so widely used in psychiatric and other patients nowadays, has been shown to mobilize the body stores of serotonin and increase its excretion. The following observations, therefore, on serotonin in the spinal fluid of patients with various neurological conditions are of considerable interest.

Quantitative analysis of the spinal fluid of 70 neurological patients has been carried out. The group included 28 patients with head injuries and 16 with brain tumors. Other disease states sampled were epilepsy, electric shock, meningitis, multiple sclerosis, ruptured cerebral aneurysm, gunshot wounds of the brain, and a scattering of other conditions. Both acetylcholine and serotonin can be assayed biologically, using the clam heart technique, because of their opposite inotropic and chronotropic effects. In addition, the specific blocking action of LSD and benzoquinone (commercially known as Mytolon) was used to identify acetylcholine and serotonin (Table 1).

FINDINGS

Acetylcholine. Acetylcholine was encountered in significant amounts in 16 of the 28 cases of head injury studied, at varying times following the injury (Fig. 1). It was never present in more than 1 or 2 μg. per cent; however, the sensitivity of the method was sufficient to make the results definite. The acetylcholine was present during the first few days following severe head injury and disappeared as the patient recovered or reached a stable neurological level, whether this represented complete neurologic recovery or not. Massive doses of atropine (2 to 6 mg.) were used in a number of patients; in a few of these, subjected to serial lumbar punctures before and after atropine, distinct reduction of the acetylcholine could be demonstrated.

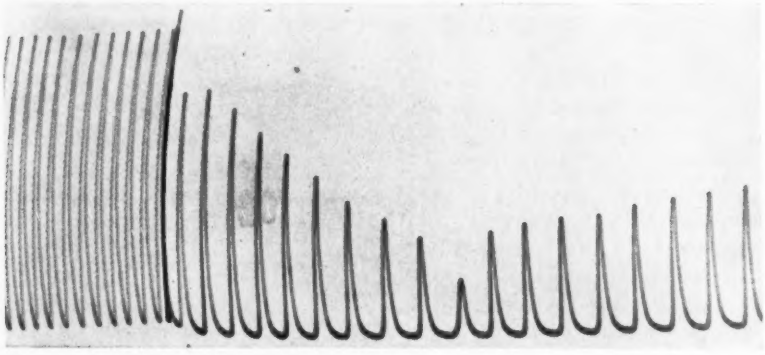

FIG. 1. Cerebrospinal fluid from patient with head injury, showing presence of *acetylcholine:* slowing heart and decreasing contractions.

As a rule this seemed to coincide with clinical improvement of the patient, but this was not always the case. In brief, this quantitative study tends to support the empirical assumption of Ward that release of acetylcholine, medication with atropine, and the patient's clinical course may be related.

Serotonin. In 6 of the 28 cases of head injuries, 5 of the 16 cases of brain tumors, and a single case of traumatic paraplegia, serotonin was found in the spinal fluid (Fig. 2). In 4 of the 6 cases of head injuries in which serotonin was recovered from the spinal fluid, it was associated with acetylcholine in the same specimens. These were separated by virtue of the selective blocking action of Mytolon and LSD. The serotonin in the spinal fluid was not associated with sufficient amounts of blood to account for its presence.

In 5 of the 16 cases of brain tumor, serotonin was demonstrated in the spinal fluid; in 2 cases it was associated with acetylcholine. In all of the cases of brain tumor, the assays were done postoperatively and the findings may simply represent another form of head injury, namely, the trauma of surgery. Serotonin was also found in the 1 case of traumatic paraplegia, and in 1 case in which no precise neurological diagnosis could be made.

In 8 cases, namely, 5 brain injuries, 2 brain tumors and 1 meningitis,

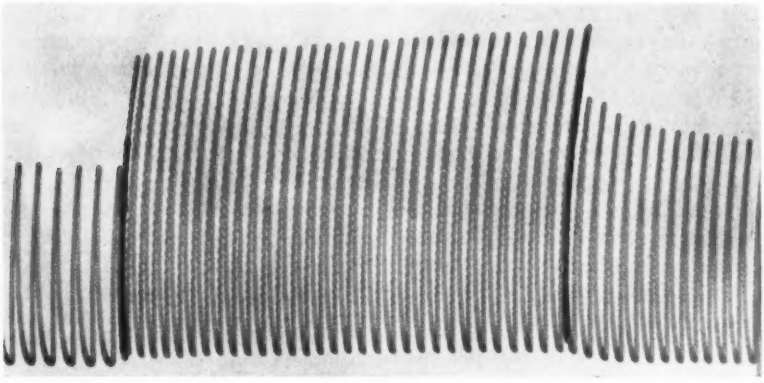

FIG. 2. Cerebrospinal fluid from patient with head injury, showing presence of *serotonin:* speeding heart and increasing contractions.

an unidentified substance was encountered in the spinal fluid. Like serotonin, it caused augmentation of the heart rate of the clam; however, unlike serotonin, it could not be blocked by LSD, and caused diminution of the contracting heart, in which respect it resembled acetylcholine. This substance has not yet been identified, but we hope to do so in the next phase of our study (Fig. 3).

Animal Experiments. Fourteen dogs and many rats have been submitted to varying degrees of quantitatively controlled concussion. Analysis of the cisternal spinal fluid of the dogs has been done by the above method. Morphine analgesia has been used because of the preservation of consciousness, as suggested by Gurdjian and Webster.[6] An air concussion gun has

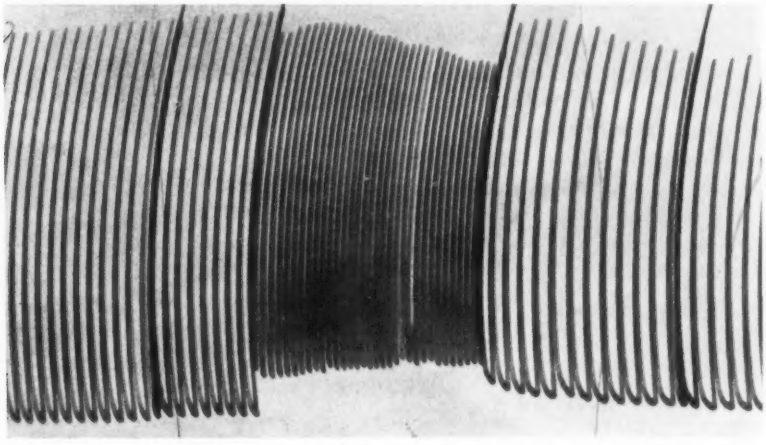

FIG. 3. Cerebrospinal fluid from patient after operation for brain tumor, showing presence of "*X*" *substance:* speeding heart and decreasing contractions.

been utilized for these experiments. Blows of variable known energies and velocities can be obtained with this instrument. The blood pressure, pulse and respiratory rates, corneal reflex, and level of consciousness have been closely followed and correlated with determinations of spinal fluid acetylcholine. Blows varying from 280- to 460-inch pounds of energy have been used so far. At the lower energies, minimum concussion was observed and no acetylcholine was found in the spinal fluid. At the higher levels of energy, severe head injuries were incurred and the majority of the animals died. In this group acetylcholine appeared in the spinal fluid as early as 10 minutes after trauma and lasted for as long as 10 days if the animal survived. Serotonin was found in 1 animal 3 weeks after trauma. The unidentified substance has not been found in any of the animals' spinal fluids analyzed so far.

DISCUSSION

The work of Bornstein and of Ward has been corroborated by quantitative acetylcholine determinations on the cerebrospinal fluid of patients with head injuries and brain tumors as well as dogs subjected to experimental concussion. The new finding of serotonin in the spinal fluid of these patients poses more questions than it answers. Brown and his co-workers[4] have shown that the cerebrovascular and cardiovascular effects of concussion and electroshock therapy are almost identical. The fact that LSD inhibits serotonin and produces psychoses suggests that serotonin may play a rôle in mental function.[3] One might postulate that since shock therapy helps some patients recover from psychoses, and since concussion and shock therapy are so similar, perhaps concussion has an anti-LSD-like effect on serotonin metabolism. This hypothesis is being tested in the laboratory by direct tissue analysis of the brain for acetylcholine and serotonin in biopsies taken from concussed rats and dogs.

SUMMARY

1. Spinal fluid acetylcholine and serotonin determinations have been done on a series of 70* patients suffering from head injuries and brain tumors and a variety of other neurologic disorders.

2. Both acetylcholine and serotonin, as well as another unidentified substance, have been found in a large percentage of these cases. Serotonin has not been reported previously in the spinal fluid of man.

3. Comparable studies on experimentally concussed animals have also been reported.

I wish to thank Prof. J. H. Welsh of Harvard University for his encouraging and helpful advice, and Miss Elizabeth Ward, who did the laboratory determinations.

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INTRADURAL LIPOMAS OF THE SPINAL CORD

WITH PARTICULAR EMPHASIS ON THE "INTRAMEDULLARY" LIPOMAS

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THE first reported case of spinal lipoma was that of Gowers[21] in 1876. Ehni and Love,[15] in 1945, were able to collect 29 cases, including 2 of their own. Since that time, cases have been reported by Collins and Henderson,[10] Barraquer-Ferré *et al.*,[4] Johnson,[26] Taniguchi and Mufson,[42] Crosby *et al.*,[11] Sarkar *et al.*,[36] and Wycis.[46] The addition of the 2 cases to be reported here, and of others already in the literature prior to 1945, brings the number of reported extra- and intramedullary lipomas to 51. The occurrence of 2 such cases within a short period of time in our own experience prompted a review of the publications since that of Ehni and Love,[15] and an analysis of all reported cases (Table 1).

CASE REPORTS

Case 1 (No. 50,305). A 15-year-old girl was admitted to the Methodist Hospital on Aug. 25, 1954, with the chief complaint of weakness of both legs and difficulty in walking. Two years previously, she had noted weakness of the right leg. Poliomyelitis was diagnosed and physiotherapy was suggested. She improved markedly so that she could walk again without difficulty. One year later she again noted impaired gait. The lower extremities felt heavy and it was hard for her to control her steps, since she could not feel the ground with the right foot. In the month prior to admission, she had pain in the right hip and numbness involving the right calf and heel. In going downstairs she was unable to balance on her right leg, which seemed to buckle at the knee; she could stand on the left leg without difficulty. Lumbar puncture performed 1 week prior to admission revealed increased cerebrospinal fluid protein; no further data were available. Following the lumbar puncture, the patient was unable to walk at all.

Neurological Examination. There were no motor, reflex, or sensory changes in the upper extremities. The right thigh measured 2 cm. less than the left. There was only minimal movement of the left leg, the right being immobile. Muscular tonus was increased bilaterally, with ankle and patellar clonus; Babinski, Oppenheim and Gordon signs were present bilaterally. Abdominal reflexes were absent. There was reduced sensation to pain, temperature and touch, more marked on the left side, from T3–4 down; two-point discrimination, position and vibration sense were lost in both lower limbs. At the level of the 3rd thoracic spinous process, there was a soft, non-tender, mobile mass, with the overlying skin thin and glistening.

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The clinical impression at this time was that of a spinal cord tumor at T2–3. The presence of a subcutaneous lipomatous mass suggested the possibility of a lipoma of the cord.

Roentgenograms of the spine in anteroposterior and lateral projections showed considerable enlargement of the spinal canal, with erosion of the pedicles and of the posterior aspect of the vertebral bodies from C5 to T4 (Fig. 1).

Operation. On Aug. 30, 1954, laminectomy was performed from C4 to T4. A mass of fatty tissue was found subcutaneously, attached to the superficial fascia in

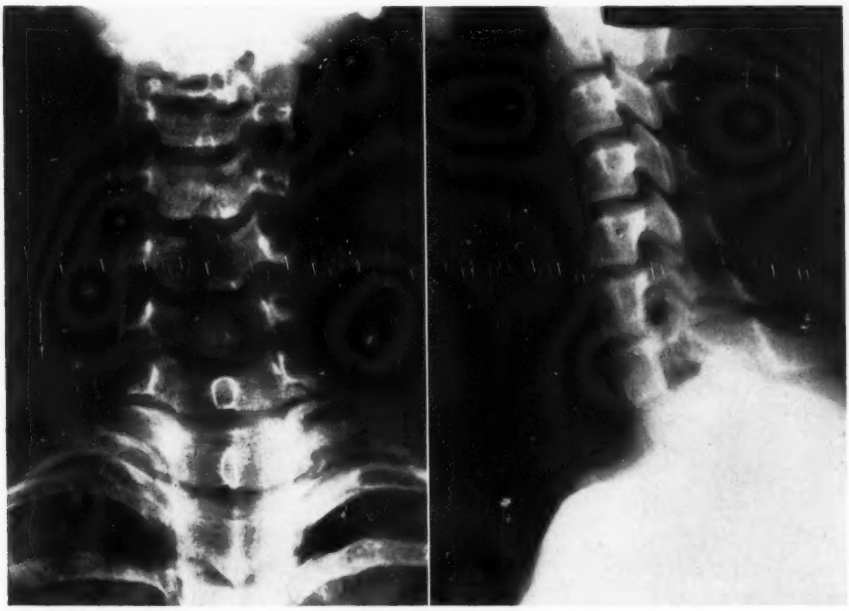

FIG. 1. *Case 1.* (*Left*) Widening of spinal canal and erosion of pedicles from C5 to T3. (*Right*) Erosion of posterior aspect of C5 through T1 vertebrae, with widening of spinal canal and alteration of normal curvature.

the lower portion of the incision; it did not penetrate beneath the bone. After removal of the laminae from C5 to T3, no dural pulsation was seen. Upon opening the dura mater, fatty tissue extending from C5 to T3 was noted completely covering the spinal cord (Fig. 2). The tumor seemed to be intimately attached to the posterior aspect of the spinal cord, was covered by pia mater, or capsule, and no plane of cleavage could be found. A 2-cm. incision was made in the midline of the tumor and carried down to a depth of 1 cm. without visualization of spinal cord tissue. The nerve roots from C5 to C8 appeared embedded in the tumor mass. No attempt at removal was made because of extreme adherence of the tumor to the spinal cord and the involvement of nerve roots. A biopsy was taken and the dura mater was left open for decompressive purposes.

Pathologic Report. Microscopic sections of the specimen revealed adult adipose tissue (Fig. 3). Also present was a well-encapsulated, mucoid tissue with sparse,

elongated cells, uniform in size and shape, suggesting clusters of neurilemma cells (Fig. 4).

Postoperative Course. There was transient urinary retention which cleared by the 7th postoperative day. The patient exhibited steady improvement in motion and sensory appreciation. On the 10th postoperative day she was discharged with the following neurological findings: she could walk with assistance, but with spastic gait; she was able to feel the ground under her feet, and there was better appreciation of superficial sensations; the reflexes remained hyperactive, with a Babinski sign and ankle clonus bilaterally.

The patient was last seen on Jan. 21, 1956, at which time she had weakness of the hand grip but could play the piano. There was weakness of the right triceps and pectoral muscles. She walked well without help and was able to stand on each foot alone. Stretch reflexes were hyperactive, with transient ankle clonus. Pain sensation was normal. Position sense was normal in the left leg, but absent in the right.

FIG. 2. *Case 1.* Operative photograph showing extent of tumor; laminectomy C5 to T3.

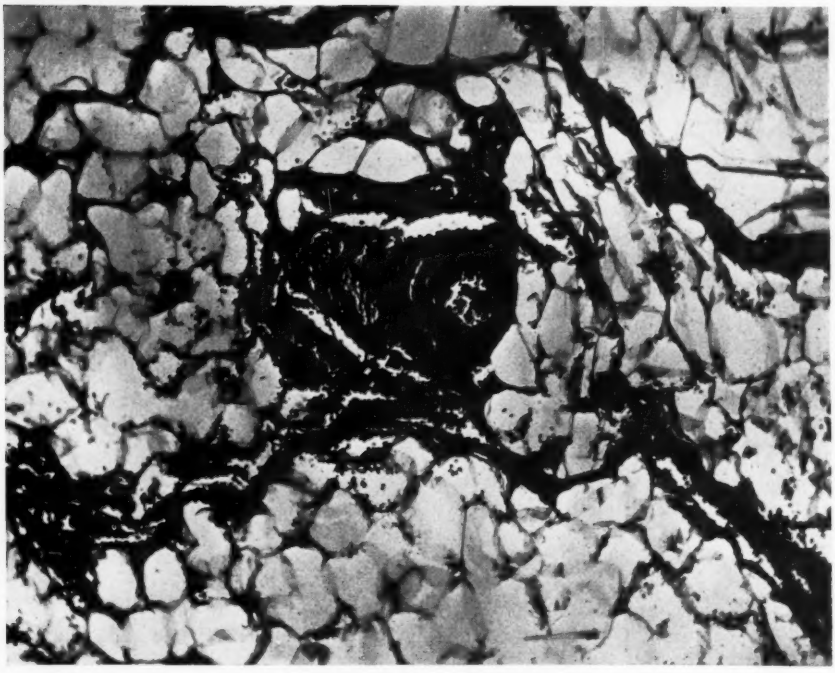

FIG. 3. *Case 1.* Biopsy, operative. Adult adipose tissue. (×100)

Case 2 (No. AR-5745). A 51-year-old colored female was admitted to the Jefferson Davis Hospital on Aug. 30, 1954, with the chief complaint of stiffness in the right leg and difficulty in walking of 4 years' duration. About 4 years prior to admission, the right knee became swollen and painful; she was treated for arthritis with slight improvement. In June, 1954, the patient fell, the right knee giving way.

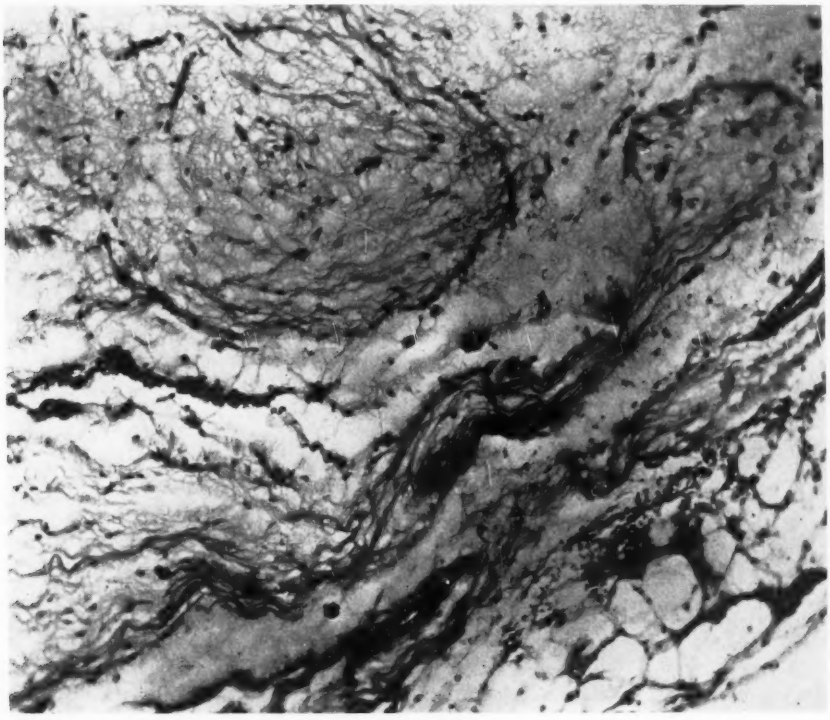

FIG. 4. *Case 1.* Biopsy, operative. Mucoid tissue, with sparse, elongated cells, suggesting clusters of neurilemma cells. (×100)

Following this, she had more trouble with the right leg, requiring a cane when walking. There was no sphincter nor sensory impairment.

Neurological Examination. Gait was spastic, more marked in the right leg. There was some weakness of dorsiflexion of the right foot and big toe. Stretch reflexes in the lower extremities were increased bilaterally, more on the right than on the left. Babinski and Chaddock signs were present on the right. There was sustained right ankle clonus. No sensory loss was noted. The impression on admission was (1) primary lateral sclerosis or (2) cord tumor.

Roentgenograms revealed scoliosis of the thoracolumbar spine, and marked degenerative disc disease affecting the thoracic spine, with hypertrophic changes anterolaterally; the pedicles appeared normal.

On Aug. 31, 1954, myelography and spinal manometric studies were done simultaneously. Jugular compression caused a rise of pressure from 160 mm. of water to 470, with sudden drop to 150 on release of the compression, interpreted as normal

FIG. 5. *Case 2.* Oblique myelogram with dye outlining lower end of tumor and block at T8.

manometrics. Myelogram disclosed a block at T8, with the table tilted to the 90° head-down position. The block had characteristics of both an intramedullary and extramedullary intradural lesion (Fig. 5). Cerebrospinal fluid contained no cells; protein was 140 mg. per cent; glucose, 69 mg. per cent; colloidal gold curve was normal; and serology was negative.

On the day following myelography, the patient fell to the floor while trying to get out of bed. It was found that she could move her toes only minimally. There was now an easily elicitable sensory level to pin prick below T5.

Operation. On Sept. 1, 1954, thoracic laminectomy was performed from T5 to T9. The dura mater was under tension and did not pulsate. On opening the dura mater, strands of connective tissue were seen between the dura mater and the underlying tumor. The tumor appeared encapsulated by a fine membrane which was continuous with the pia mater of the cord. A plane of cleavage was found inferiorly and an attempt was made to develop this further. Removal of the tumor *in toto* was soon found to be impossible because of the infiltration of the cord by fatty tissue. However, all but minute portions attached to the cord were removed by a piece-meal attack. The posterior roots of T7 and T8 were seen embedded in the tumor tissue and were severed to facilitate this procedure.

Pathologic Report. Microscopic sections of the specimen revealed well-differentiated adipose tissue containing a few small blood vessels and two nerve roots. A diagnosis of lipoma of the spinal cord was made.

Postoperative Course. The patient was able to move her legs immediately following operation. Headaches and stiff neck were noted for several days. Lumbar puncture revealed xanthochromic fluid; no organism was found on smear and culture of the cerebrospinal fluid. A Foley catheter was required for 1 week, but she voided well thereafter. The patient had hypalgesia from T6 down on the right side. Stretch reflexes were hyperactive bilaterally, with a Babinski sign and ankle clonus on the right. She gradually regained strength in both extremities during the following days, so that 10 days postoperatively she was able to stand and walk with help. The patient was discharged 24 days after surgery with unsteady spastic gait, hyperactive reflexes in the lower extremities and a Babinski sign and ankle clonus on the right.

She was last seen on April 13, 1956, there having been progressive improvement to that date. There was weakness and spasticity of the right leg. Reflexes were still hyperactive, with Babinski sign and ankle clonus on the right. Position-sense was absent in the right leg. No other sensory change was noted. The patient was able to walk with the aid of a cane and was working.

DISCUSSION

1. *Origin and Pathology.* The nature of these lesions has been controversial and no authoritative information is available as to the exact site of

TABLE 1

SUMMARY OF 51 CASES OF INTRASPINAL LIPOMAS*

Case No.	Author Year	Sex Age	Location	Pathology	Associated Lesions	Surgery and Course	X-ray Findings	Myelogram
1	Gowers[21] 1876	—	Conus	Capsule of pia	Tabes	Necropsy		
2	Braubach[3] 1884	F 5	C5 to T4	Rt. posterior surface. Proliferation of stroma with extension into cord		Necropsy		
3	Turner[43] 1888	F 54	Midthoracic posteriorly	Lt. side. Pia thickened and cellular; cellular fibrous tissue sending strands into cord	Obesity	Necropsy		
4	Spiller[39] 1899	F	Filum terminale	No invasion	Tabes	Necropsy		
5	Root[34] 1906	F 43	Midthoracic posteriorly	No extension into cord		Tumor removed. Improvement. Death 2 yrs. later of pneumonia		
6	André-Thomas & Jumentié[1] 1912	M	L5 to S5	Invasion and destruction of cord by fibrous tissue		Necropsy		
7	Wolbach & Millet[45] 1913	M 10 mos.	Entire cord to cauda equina	Fibrous extension into cord	Intracranial lipoma. Hydrocephalus. Harelip. Absent rt. kidney	Necropsy		
8	Oppenheim & Borchardt[30] 1918	M 44	C1 to C4, midline posteriorly	Lipomatous extension into cord		Subtotal removal. No improvement		
9	Ritter[32] 1920	M 43	C1 to T1	Rt. posteriorly. Pial septum between tumor and cord, sending cellular strands into cord	Kyphoscoliosis. Hydrocephalus	Necropsy	Kyphoscoliosis	
10	Henneberg[23] 1921	—	Cervical, midline posteriorly	Heavy strands of connective tissue penetrating cord		Necropsy		
11	Elsberg[17] 1925 (Case 1)	F 11	C8 to T2	Lateral surface anterior to dorsal roots. Extramedullary	Kyphosis	Two-stage removal. Patient walking 4 yrs. later	Kyphosis & arthritis	
12	Elsberg[17] 1925 (Case 2)	F 19	T2 to T4	Extramedullary		Total removal, 2 stages. Recovery		
13	Stookey[40] 1927	M 11	C2 to T5	Extradural, intradural & intramedullary	Subcutaneous lipoma over intraspinal lesion	Partial removal. Improvement. 3 yrs. later, recurrence	Widening of spinal canal	

* Cases 1 through 19, and 24 through 31, are from the review by Ehni and Love[15] in 1945.

TABLE 1—*Continued*

Case No.	Author Year	Sex Age	Location	Pathology	Associated Lesions	Surgery and Course	X-ray Findings	Myelogram
14	Bielschowsky & Valentine[7] 1927	M 1	T11 to S4, posteriorly	Thickened pial strands with cord invasion	Hydrocephalus. Hydromyelia. Club feet. Pseudohermaphroditism. Cataracts	Necropsy		
15	Sachs & Fincher[35] 1928	M 46	T7 to T8, dorsal inferior	Intramedullary		Total removal. Death 8 yrs. later, cause unknown		Suggestive block
16	Fay[18] 1928	F 21	T3 to T7, posteriorly	Superficial invasion of cord		Capsule incised, death in 3 mos.		
17	Beykirch[6] 1928	M 36	Cauda equina	Minimal stroma with few nuclei		Necropsy		Block
18	Furiosi[19] 1930	M 6	Filum terminale			Necropsy, incidental finding		
19	Kernohan *et al.*[27] 1931	M 19	C4 to T1, midline	Extramedullary		Partial removal. Complete recovery. Recurrence 9 yrs. later		
20	Robineau[33] 1932 (Case 1)	F 14	C1 to T4, posteriorly	Posterior aspect of cord split with tumor protruding		Subtotal removal in 2 stages; slight improvement		
21	Robineau[33] 1932 (Case 2)	M 28	T? to T7	Spinal cord infiltration		Partial removal; 1 yr. later patient's gait improved		
22	Robineau[33] 1932 (Case 3)	M 33	Thoracic, superior anterior lt.	Extramedullary		Removal of tumor; 2 yrs. later, no improvement		
23	Robineau[33] 1932 (Case 4)	M 40	Thoracic, inferior	Rt. posterior spinal cord invasion		Partial removal. Improvement 6 mos. later		
24	Eckart[13] 1935	F 30	Midcervical to lumbar			Necropsy		
25	Stotz[41] 1935		Insufficient data	Fibrolipoma with destruction of whole thickness of cord		Necropsy		
26	Dobrokhotoff[12] 1936	F 25½	Cervical to lumbar			Necropsy		
27	Scherer[37] 1936	F 41½	C4 to T5, rt. dorsal			Partial removal. Died of meningitis after 3rd operation. Necropsy		

TABLE 1—*Continued*

Case No.	Author Year	Sex Age	Location	Pathology	Associated Lesions	Surgery and Course	X-ray Findings	Myelogram
28	Guillain *et al.*[22] 1937	F 52	T5 to L5, entire dorsal surface	Fibrous tissue infiltration. Dorsal columns destroyed		Necropsy		
29	Baker & Adams[5] 1938	F 1	Entire cord, posteriorly	Dense membrane separating tumor from cord	Hydrocephalus. Intracranial lipoma. Defect of GU tract. Xanthoma eyelids	Necropsy		
30	Bucy & Gustafson[9] 1939	M 18½	C1 to C4, posteriorly	Dense capsule	Pilonidal cyst. Lipoma of neck over deep lesion	Subtotal removal. Excellent results	Widening of spinal canal	Block
31	Jabotinski[24] 1939	F 13 mos.	C1 to C8, dorsal surface	Fibrous tissue proliferating and sending extensions into cord		Necropsy		
32	Wilson *et al.*[44] 1940	F 21	T2 to T6	Posterior aspect of cord. Tumor intimately attached to cord without demonstrable limiting membrane on deep surface of tumor		Biopsy. Died 3 mos. later. Necropsy (pyelonephritis)		
33	Jaeger[25] 1941	M 28	T2 to T5	Intramedullary		Total removal. Recovery		Block
34	Riser *et al.*[31] 1942	M 41	T10 to T11	Intramedullary		Total removal. Excellent result		Defect
35	Ehni & Pugh[16] 1944	M 41	T6 to T11	Lt. posterior. Extramedullary with capsule of collagenous connective tissue	*Café au lait* spots in rt. loin	Decompression. Slight improvement		
36	Ehni & Love[15] 1945 (Case 1)	F 20	T7 to T11	Posterior aspect of cord. Extension of connective tissue into cord	Obesity. Pilonidal cyst. Extradural lipoma	Partial removal. No improvement	Thinning of pedicles; erosion of vertebral bodies	
37	Ehni & Love[15] 1945 (Case 2)	M 43	T9 to T10	Rt. dorsal roots, surrounded by connective tissue	Obesity. Extradural lipoma. Pilonidal cyst	Total removal. Present status unknown	Erosion of pedicles	Defect
38	Ehni & Love[15] 1945 (Case 3)	M 22	C7 to T6	Rt. posteriorly. Lipoma slightly fibrous		Laminectomy. No removal	Erosion of pedicles	
39	Asenjo[2] 1945 (Case 1)	M 1	C2 to cauda equina	Posterior aspect of cord		Decompression. Died 2 days later. Necropsy		Block
40	Asenjo[2] 1945 (Case 2)	M 44	T8 to T10	Extramedullary. Posterior aspect of cord capsule		Total removal. Improvement		
41	Furtado & Marques[20] 1946	F 59	Cauda equina posteriorly		Lipoma over tumor	Partial removal		
42	Meltzer[29] 1947	F 33	Midline, lower cervical		Ivory vertebrae	No remova	Ivory vertebrae	Block

TABLE 1—*Continued*

Case No.	Author Year	Sex Age	Location	Pathology	Associated Lesions	Surgery and Course	X-ray Findings	Myelogram
43	Collins & Henderson[10] 1949	F 48	C7 to T6	Adherent to cord		Laminectomy. Decompression, and death (?)	Kyphoscoliosis	Block
44	Johnson[26] 1950	F 64	T5 to T8	Intramedullary	Subcutaneous lipoma over spinal tumor	Partial removal. Slight improvement. Residual evidence of transverse cord lesion	Widening of spinal canal with scoliosis	Partial block
45	Barraquer-Ferré *et al.*[3] 1950	M 21	T3 to T9	Posterior. Intramedullary. Adhesions between cord and tumor		Subtotal removal. Great improvement after 2 yrs.		Block
46	Taniguchi & Mufson[42] 1950	M 52	T11	No delimitation between tumor and cord	Syringomyelia	Partial removal. No improvement		Intraspinal mass
47	Wycis[46] 1953	F 48	C7 to foramen magnum	Intramedullary	Klippel-Feil syndrome	Decompression. Improvement	Widening of spinal canal	Block
48	Crosby *et al.*[11] 1953	F 31	T7 to T11	Extramedullary		Total removal in 2 stages. Improvement		Block
49	Sarkar *et al.*[38] 1953	F 20	C6 to T6	Intramedullary		Decompression. Improvement	Widening of spinal canal	Block
50	Caram *et al.* 1956 (Case 1)	F 16	C7 to T4, posteriorly	Intramedullary	Subcutaneous lipoma over cord lesion	Partial decompression. Improvement	Widening of spinal canal with erosion of vertebral bodies	Not performed
51	Caram *et al.* 1956 (Case 2)	F 63	T5 to T7	Extramedullary		Total removal. Improvement	Scoliosis, arthritis	Block

origin and further evolution. It has been generally accepted that lipomas are mesenchymal, not neural, in origin,[28] this concept being supported by the absence of glial tissue in the tumor mass. It is thought that they may derive from lipoid cells already present in the pia mater, or from fatty transformation of connective tissue. The lipomas may infiltrate neural tissue by propagation of fibrous strands carrying fatty cells into the spinal cord. Likewise, because of their location on the dorsal aspect of the cord, they may split the posterior columns, giving the impression that the tumor has originated within the cord. Another source of confusion is the occurrence of intimate adhesions between the capsule of the tumor, which usually covers the lipoma, and the pia mater of the spinal cord, making it difficult to find a delimitation between tumor and neural tissue.

Because of these peculiarities, it appears that, at least from the surgical point of view, the tumors behave as intramedullary lesions, although their

TABLE 2

Associated lesions with intraspinal lipomas

Subcutaneous lipoma	5	Pilonidal cyst	2
Extradural lipoma	2	Syringomyelia	1
Intracranial lipoma	2	Hydromyelia	1
Hydrocephalus	4	Klippel-Feil syndrome	1
Harelip	1	Club feet	1
Cataracts	1	Tabes	2
Xanthoma of eyelid	1	Kyphosis	1
Absence of right kidney	1	Kyphoscoliosis	2
Pseudohermaphroditism	1	Osteoarthritis	1
Defect in genitourinary tract	1	Obesity	3

origin may be more truly extramedullary. On microscopic examination, the tumors were found to be composed entirely of adult adipose tissue, with no evidence of embryonal fat cells. In occasional instances, the lipoma was extremely vascular with hemangiomatous characteristics. The congenital origin of the lipomas was suggested by their frequent occurrence early in life and by the numerous associated anomalies (Table 2).

2. *Location.* Such tumors generally had a tendency to extend longitudinally, occupying several segments of the cord. Of the 51 cases reviewed the tumors were located as follows (Fig. 6): 6 in the cervical region; 11 in the cervicothoracic region; 20 in the thoracic region; 5 in the conus and cauda equina; 1 in the thoracolumbar region; 1 extending from thoracic to sacral region; 1 in the lumbosacral region; in 5 cases the tumors occupied the entire length of the spinal cord from the cervical region to the cauda equina; and in 1 case, localization could not be determined (Case 25). The thoracic area appeared to be most frequently involved (38 per cent).

3. *Sex and Age Incidence.* There were 27 males and 24 females, an insignificant sex difference. Of 51 patients, 6 were from 1–10 years of age; 10 were from 11–20; 8 were from 21–30; 5 were from 31–40; 11 were from

41–50; 5 were from 51–60; 1 was between 60 and 70; in 5 the age was not reported. Of the 5 patients with widespread tumors involving the whole cord, 2 patients were adults and 3 were under 1 year of age.

4. *Clinical Course.* The clinical course of a spinal cord lipoma was typically one of slow progression with occasional temporary remission. It has been postulated that such remissions could be related to changes in the systemic metabolism of fat with loss of weight.[5] No such correlation was noted between obesity and symptoms; obesity was found in only 3 of 51

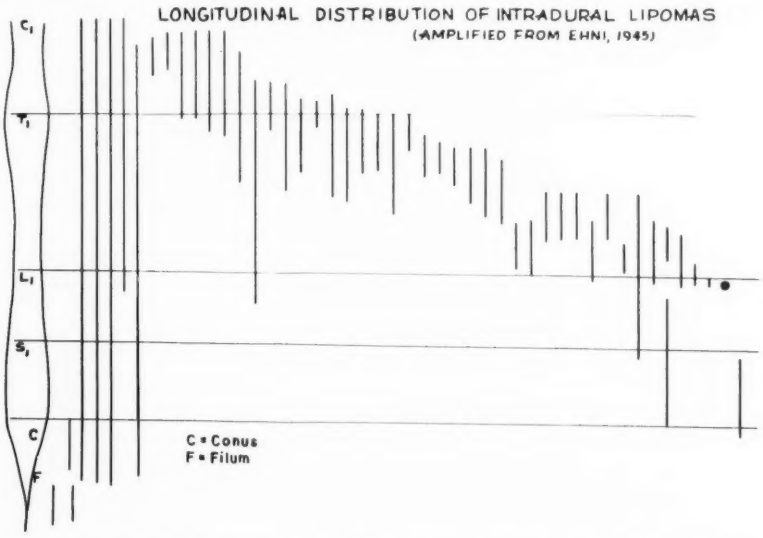

FIG. 6. Longitudinal distribution of intradural lipomas. (Amplified from Ehni and Love[15])
● = D11 segment only.

cases, while the variability in symptomatology occurred with much higher frequency, the remissions not being associated with loss of weight.

The occurrence of remissions, alternating with recrudescence of symptoms, may in some instances be misleading and make the diagnosis difficult until signs of spinal cord compression become quite evident.

Numerous clinical diagnoses have been made during the course of these lipomatous tumors, with syringomyelia (Cases 44 and 46), posterolateral sclerosis (Case 32), poliomyelitis (Case 50), amyotrophic lateral sclerosis (Case 51), and tabes dorsalis (Cases 1 and 3) the most frequent. A preoperative diagnosis of lipoma of the spinal cord has been made in only a few cases (Cases 35, 47, and 50).

Among the 51 cases reviewed, the following associated lesions were observed: obesity in 3 instances (Cases 3, 37 and 43); intracranial lipoma and hydrocephalus in 2 cases (Cases 7 and 29); hydrocephalus alone in 2 cases (Cases 9 and 14); subcutaneous lipoma at the same level of the spinal

lesion in 5 cases (Cases 13, 30, 41, 44, and 50). Less common associated abnormalities were absence of one kidney and harelip (Case 7); kyphoscoliosis or kyphosis (Cases 9, 11, 51); pilonidal cyst (Cases 30 and 37); Klippel-Feil syndrome (Case 47); hydromyelia, club feet, pseudohermaphroditism, cataracts and hydrocephalus (Case 14); and *café au lait* spots (Case 34).

It is difficult, therefore, to delineate a clinical picture that is suggestive of a spinal cord lipoma. Thus, the age incidence, long duration of symptoms, absence of radicular pain, spastic gait with flaccid paresis of the upper extremities, and the radiographic evidence of erosion and/or widening of the spinal canal, all are nonspecific findings noted in association with a variety of cord neoplasms. However, the presence of a subcutaneous lipoma overlying the suspected clinical level (10 per cent) in such a patient with cord compression, may lead to the clinical diagnosis of an associated intraspinal lipoma.

5. *Roentgenographic and Cerebrospinal Fluid Findings.* The roentgenograms showed widening of the spinal canal (Cases 13, 30, 44, 47, 49 and 50), erosion of the pedicles and vertebral bodies (Cases 36, 37, 38 and 50), scoliosis and kyphosis (Cases 9, 11 and 51), and arthritis and ivory vertebrae (Case 42). Such alterations alone were not of diagnostic value, but their association with lipomas might be significant and aid in the clinical diagnosis.

Lumbar puncture and cerebrospinal fluid studies revealed the characteristic findings of cord compression, with increased spinal fluid protein and eventual presence of block. It is of interest that manometric studies were normal at times, although subsequent myelogram revealed a complete block (Cases 34, 37, 45 and 51). From the myelographic point of view, these tumors had radiographic attributes of intradural extramedullary or intramedullary tumors, or of both (Case 51). This correlates well with the peculiar way in which the lipomas grow or extend into the spinal cord, even if true pathological infiltration has not been demonstrated. The myelogram was of value in the diagnosis of spinal cord tumor in the following reported cases, the most common defect suggesting an intramedullary neoplasm (Cases 15, 17, 30, 33, 34, 37, 39, 42, 43, 44, 45, 46, 47, 48, 49 and 51).

The aggravation of the clinical signs following lumbar puncture is of interest. The first patient (Case 50) became almost completely paraplegic following the lumbar puncture; the second (Case 51) exhibited aggravation of the pre-existing paraparesis, and a sensory level, not previously elicited, appeared the day following myelography. This was also true of Case 11, a patient who had only a spastic paraplegia, but in whom total anesthesia developed up to the 4th thoracic dermatome following lumbar puncture; and of Case 16, a patient with spastic paraparesis and impaired vibratory and position sense, who following lumbar puncture had increased deficit in vibratory and position sense, as well as impaired pain and temperature sense below the 6th thoracic segment. Such exacerbation of signs may occur, of

course, following lumbar puncture in cases of non-lipomatous spinal cord tumors.

6. *Mortality.* Many of the reported cases of spinal cord lipomas were necropsy observations; in 15 of 51 cases, or 30.5 per cent, the tumors were found at autopsy. An attempt was made to correlate the presence of spinal cord lipomas with the cause of death in these cases. In 2 cases, there were associated multiple anomalies incompatible with life; in 2 other cases there was a diagnosis of tabes dorsalis and the luetic infection probably accounted for the death. In the remaining 11 cases, the lipomas were incidental autopsy findings.

7. *Surgical Approach.* Laminectomy was performed in the 36 cases in which the clinical diagnosis was spinal cord tumor. In 10 of these cases, the tumor was removed *in toto* (Cases 5, 11, 12, 15, 22, 33, 34, 37, 48 and 51), the tumor being extramedullary in 5, and intramedullary in 5. In 2 of these cases (Cases 11 and 12), total removal was accomplished in a two-stage operation. Improvement was reported in each instance, except in 1 (Case 37), in which the late result was unknown. Further follow up of these cases indicated that 1 patient (Case 5) died 2 years after the operation because of pneumonia; another (Case 15) died 8 years later following an unrelated operation.

In 14 cases (9 intramedullary; 2 extramedullary; 2 of the cauda equina; 1 of unknown location) partial removal of the tumor was performed. Six of these patients showed marked improvement to complete recovery; in 7, there was only slight if any improvement; 1 patient (Case 41) died at the time of operation because of uremia.

In 12 cases only, a decompressive laminectomy with biopsy of the tumor was performed. Four of these patients died following the operation; the tumor was extremely extensive, from T11 to S4 in 1 case (Case 14), and associated with the cord lesion there were hydrocephalus, hydromyelia, club feet and pseudohermaphroditism; in 2 cases (Cases 16 and 43) the cause of death was unknown; the fourth patient died 3 months after the operation because of pyelonephritis. In 5 of these 12 cases there was marked improvement to complete recovery; in 1 case, slight improvement occurred. In 2 cases, the result was unknown.

It appears evident that improvement has been reported after any type of surgical procedure performed, from simple decompression to total removal. It seems understandable that when the spinal cord compression is relieved, even by simple decompression, improvement may occur, but sooner or later the symptoms will recur. The best results were in those cases in which total removal was performed. When a clear plane of cleavage is found, the removal of the tumor is a simple matter; on the other hand, in those cases in which the tumor is firmly attached to the cord, or the fibrous extensions into the cord are numerous, total removal is difficult or impossible. In these latter cases, the capsule should be opened and the tumor should be removed piece-meal, leaving the capsule attached to the spinal cord.

The operative results in the reported cases of lipomas of the spinal cord were not completely satisfactory. This is because of the nature of the lesion

itself, particularly its great longitudinal extent, the difficulty in delineating the tumor from neural tissue, and the resulting lack of an adequate plane of cleavage. It is hoped that a more complete removal prior to extensive involvement of the cord will yield more gratifying results.

SUMMARY

1. Fifty-one cases of intramedullary lipomas have been reviewed and their origin, pathology, localization, and clinical and radiological aspects are discussed.

2. Associated abnormalities are enumerated, and the possibility of a preoperative etiological diagnosis is suggested.

3. Surgical treatment of these tumors is discussed and the postoperative results are considered in light of the type of procedure performed. Total removal, when possible, gave the best results, but even simple decompression allowed improvement in some cases.

The authors would like to thank Dr. James Greenwood, Jr. for his kind permission to allow the inclusion of Case 1. The guidance and criticism of Dr. George Ehni is gratefully acknowledged.

ADDENDUM

Since the submission of this paper, Slade and Vinas[38] have reported the case of a 17-year-old colored female with progressive paraplegia. Myelogram revealed a block at T4. Three laminectomies were performed in an effort to remove the tumor, which was ultimately felt to be intramedullary and inoperable; a biopsy was obtained. Definite improvement occurred between operations, but ultimately she became incontinent of bladder and bowel. Anterior rhizotomy was required for relief of mass reflexes.

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EXPERIMENTAL OBSERVATIONS ON THE PREVENTION OF SEIZURES BY INTRAVENOUS PROCAINE INJECTIONS*

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ALTHOUGH great strides have been made in the treatment of epilepsy, a continuous and vigorous search is being made widely for new agents that may supply some additional measure of control to aid patients suffering from this severely incapacitating disorder. For this reason, it was felt appropriate to report experimental observations made recently concerning transient, but very effective anticonvulsive properties of procaine hydrochloride.

During the course of a series of experiments on cortically induced seizure discharge in monkeys, it was found that convulsions could not be elicited even from most highly epileptogenic zones if the animal had been given an intravenous injection of procaine preceding the application of the initiating stimulus. This protection persisted for upwards of 30 minutes and apparently did not depend upon the induction of a somnolent state in the animal. These observations were extended by testing the capacity of procaine and related agents to protect monkeys against seizures induced by a technique identical with that employed clinically in electroshock therapy.

During the course of these studies, it came to our attention that the phenomenon under investigation has been noted and extensively explored recently by Bernhard and Bohm[1] in Sweden and that attention is being given it elsewhere.[13,14] The observations reported here confirm in general the protective effects of procaine hydrochloride against experimentally induced seizures.

EXPERIMENTAL PROCEDURE

Initial observations were made upon 2 monkeys (*Macacus mulatus*) in which the seizure was elicited by a stimulus (5–15 V., 50 c./sec., 1 msec. for 3 sec.) applied directly to the premotor cortex. The craniectomy exposure had been made under ether anesthesia, the areas of pressure and incision being injected with Novocain. The anesthesia was terminated and the animal was immobilized by curare (d-tubocurarine), respirations being maintained artificially. Recordings of seizure activity

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were made on a Grass Model III EEG amplifier and ink-writer (8 channels) from bipolar concentric nicrome wire electrodes inserted stereotaxically into deep structures and from silver ball electrodes applied directly to the cortex. For control, a diffuse seizure was elicited by cortical stimulation. Subsequently, 10 ml. of procaine hydrochloride were injected intravenously in 1 min., throughout which time electroencephalographic tracing was made. The stimulus was then reapplied immediately and at 10-min. intervals after the completion of the injection, the effect upon the electroencephalographic tracing being recorded.

Subsequent observations were made upon 10 normally wakeful monkeys secured to an animal board by a specially devised head holder and by restraints of extremities. Bipolar electroencephalographic recordings were made between needle electrodes, one applied to each frontal and each parietal region in the calvaria. The seizure-inducing stimulus was applied bitemporally from an Offner Electric Shock Therapy Apparatus, Type 732. Initial assessments were made upon 3 animals to determine the optimum parameters of stimulus for inducing reproducible seizures. In these experiments, 200 to 600 mA. of 0.1 to 0.4 sec.' duration were evaluated, but for the study itself, a current of 200 mA. for 0.2 sec. was consistently employed.

In each experiment, an initial shock was applied so that the nature and duration of the recorded and observed seizure could be noted for control. When the record had returned to a pre-stimulus state and the animal appeared normal again, the drug to be tested was injected intravenously (usually within a period of 2 min.) during continuous electroencephalographic recording. The response of the animal to the shock was then tested in 5 min. and at 5- to 10-min. intervals thereafter until the induced seizure again approximated that resulting from the control stimulus.

In the course of the study, the effects of procaine hydrochloride, procaine amide, Xylocaine,* para-aminobenzoic acid and dimethyl-aminoethanol were evaluated. In some instances two drugs were tested successively and even repeatedly during the same experiment in order to compare, particularly, the protective effect of procaine after a different substance had proved ineffective in blocking a seizure. Additionally, some animals were used for repeated experiments after it was observed that the injections or shocks had no prolonged or deleterious effects upon them. In all, 27 injections were evaluated in 10 animals.

RESULTS

Initially, it was necessary to determine optimum parameters of a stimulus that would induce constantly reproducible seizures in each animal at regular (preferably short) intervals. It was found that the nature and duration of a seizure excited in different animals varied somewhat but, with threshold excitation, the convulsive episode for each individual subject remained quite constant. Increasing the strength of current above 200 mA. and the duration of the stimulus above 0.2 sec. prolonged the tonic phase of the discharge somewhat but did not otherwise alter its appearance. Moreover, the reproducibility of seizures was not significantly affected by the interval at which shocks were applied so long as this interval remained above 5 min. Thus, a characteristic convulsive attack for each subject could

* Xylocaine, Astra. (dimethyl aminoacetate, lidocaine).

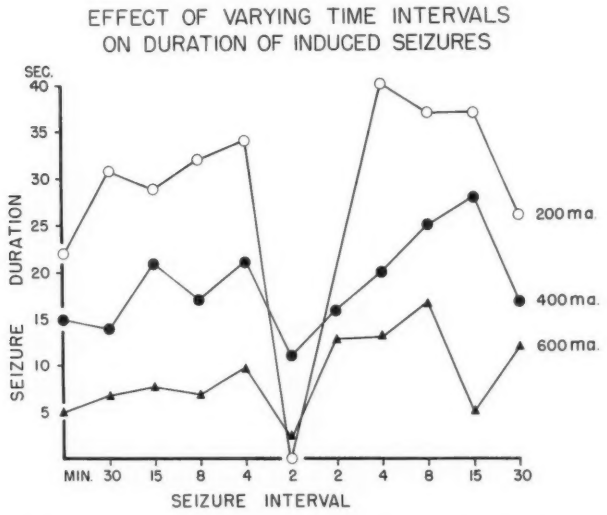

FIG. 1. Graphs indicating the effect of shortening or lengthening intervals between stimuli upon the duration of seizures induced in 3 animals by applications of electroshocks of 200 to 600 mA. intensities and of 0.2 sec. duration. Note that the comparable convulsions were reproducible by all current strengths so long as induction interval was not shortened to more than 4 minutes.

be excited with considerable regularity if the period between shocks was shortened progressively from 30 to 5 min., regardless of the intensity of current utilized. If the interseizure period was shortened beyond this point, however, the convulsive attack that resulted was often brief or was occasionally blocked (Fig. 1). For these reasons, a stimulus of 200 mA. for 0.2 sec. was utilized in all subsequent tests. Fig. 2 indicates that an animal sub-

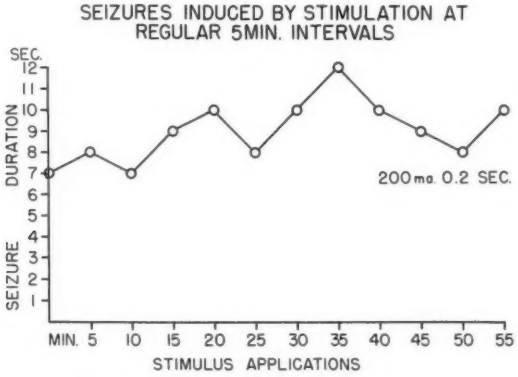

FIG. 2. The graph demonstrates the consistency with which convulsions of comparable duration could be elicited by application of electroshocks (200 MA., 0.2 sec.) every 5 minutes.

jected to such shocks at regular 5-min. intervals for nearly an hour exhibited consistent convulsive responses.

The protective effect of intravenous procaine is illustrated in Fig. 3 by electroencephalographic records made from the same animal following stimuli at comparable intervals before and after injection. In contrast with the control test, the tracing exhibited no seizure discharge 1 and 15 min. after the administration of procaine and simultaneous behavioral observations

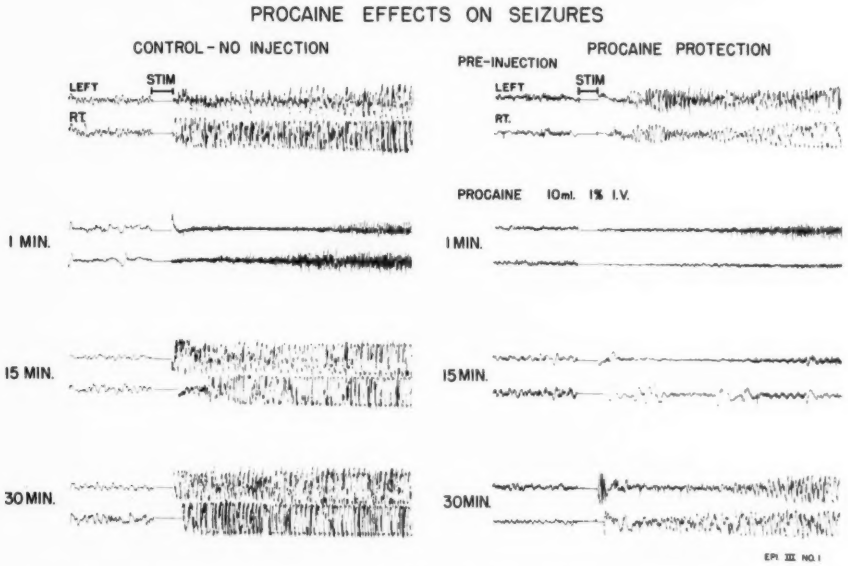

FIG. 3. These electroencephalographic tracings from the left and right (RT) hemispheres of a monkey show the effect of intravenous procaine upon induced seizures. Control tests in the left column revealed that seizure discharge followed each stimulus. Contrastingly, seizures were completely inhibited until 30 minutes after injection of procaine (right column).

failed to reveal either a change in the alert state or the onset of convulsive movements in the animal. This protective capacity of procaine was investigated in 16 instances (Fig. 4). On 9 occasions, procaine was the first drug tested, while in 7 experiments it was administered after a previously injected substance had afforded either incomplete or no protection against the induced convulsion. It was possible to demonstrate complete protection by procaine from seizure discharge on 12 occasions and partial protection on 2 others. In only 2 instances was no protection exhibited and in both of these it is possible that a previously injected agent interfered with its seizure-inhibiting action.

Since Xylocaine is known to have twice the potency of procaine as a local anesthetic, 0.5 per cent solutions of this drug were utilized and a similar

concentration of procaine amide was employed. Stoechiometric concentrations of the other substances (0.5 per cent solutions) were injected.

The injection of procaine was attended by transient changes in the behavior of the animal and in its electroencephalogram (Fig. 5). Usually no change occurred until 5–7 ml. (12–17 mg./kg.) had been delivered, after which the monkey became quiet and the electroencephalographic tracing tended to exhibit a minimal increase in relatively high-voltage synchronous activity. There was no significant change in the record after 10 ml. (25–30 mg./kg.) had been injected, but characteristically the animal appeared to be "dopey" and frequently it was difficult to excite its attention. On occasion the subject could not be aroused temporarily, but even in such rare instances, the depressed state was not reflected in a hypersynchronous electro-

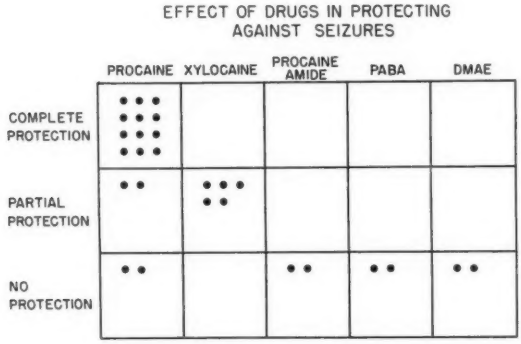

FIG. 4. The graph indicates the high degree of protection afforded by procaine and the partial effect elicited by Xylocaine. The other agents proved ineffective.

encephalogram, and the animal was always alert within 5 minutes. When the shock was applied, after such injection, the animal would stiffen for the instant the stimulus was on. However, it would not convulse or lose consciousness; rather, it would chirrup angrily and strain in an effort to break its restraints.

Because the protective effects of procaine hydrochloride could be repeatedly and consistently demonstrated, it was determined to investigate possible similar capacities of other agents that were closely related chemically either to the entire procaine molecule or to its component parts (Fig. 4). Two procaine-like substances tested were Xylocaine and procaine amide.

Xylocaine, having twice the clinical potency of procaine, was injected as 0.5 per cent solution. Even when so diluted, this substance proved to be more toxic than procaine and to have a distinctly lower margin of safety. Some suggestion of synchrony developed in the electroencephalographic tracing even when less than 5 ml. (6–8 mg./kg.) had been injected (Fig. 5, line 2) and occasionally diffuse spiking was evident at this stage. Concur-

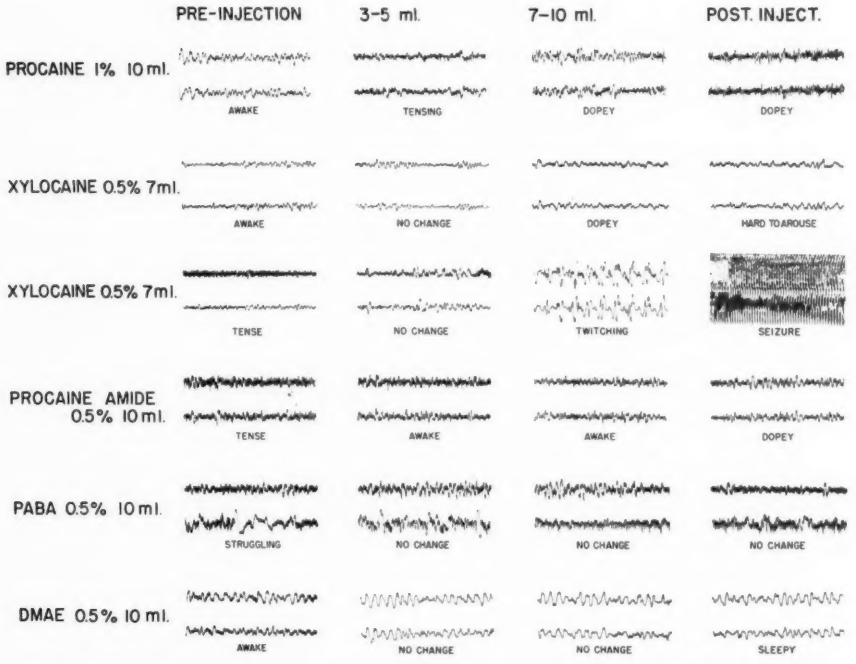

FIG. 5. These tracings from left (upper channel) and right (lower channel) sides of head illustrate effects exerted on the electroencephalogram of each substance tested in the animals. The descriptive term below each record indicates the observed behavioral state of the animal at the time the tracing was made.

rently, the animal appeared "dopey" and "drunk," commonly exhibiting gross nystagmus. With larger amounts, it became stuporous and, while this state was transient, the monkey was more deeply depressed than with larger amounts of procaine. On two of five occasions in which the drug was tested, seizure activity began when 7 ml. (8–10 mg./kg.) had been injected. In one instance, more Xylocaine was administered and the animal was thrown into a state of protracted convulsive episodes which persisted for 30 min., at which time Nembutal was administered and the seizures stopped (Fig. 5, line 3).

Complete protection against induced seizures was never observed in the five tests made using Xylocaine. In all instances, however, the duration of the seizure was significantly shortened for as long as 30 min. (Fig. 6). This partial protection, as with procaine, did not depend upon prolonged depression of the observed behavioral state or upon the appearance of electroencephalographic synchrony, as the animal appeared attentive following the

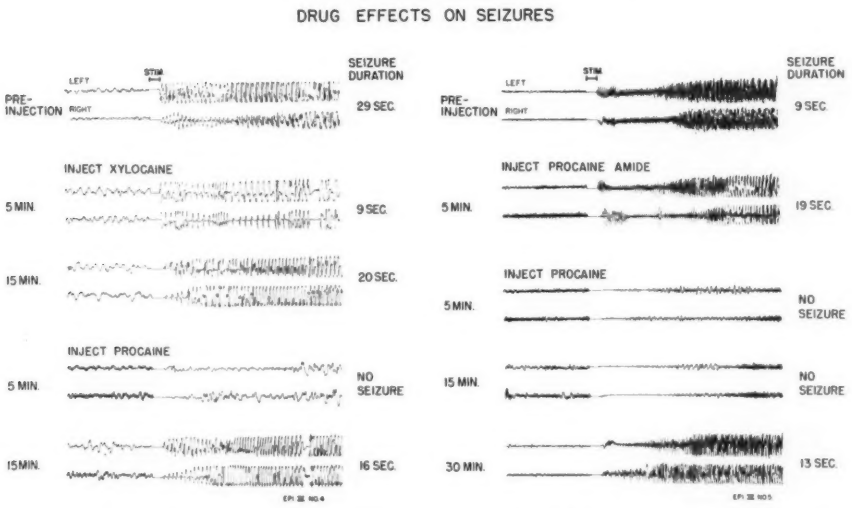

FIG. 6. Partial protection of Xylocaine is indicated by tracings in left column. Subsequent complete protection afforded by procaine injections indicates its greater protective potency. Similar comparison is apparent for procaine amide and procaine, illustrated in right column, except that procaine amide induced no protection whatever.

transient stupor at the completion of injection and its record exhibited little abnormality if spontaneous seizures did not develop. That procaine itself, however, was definitely more effective than Xylocaine in inhibiting seizures was indicated by the fact that complete protection could be afforded upon the administration of procaine to an animal immediately after the period of partial protection of Xylocaine had ended (Fig. 6).

Another modification of the procaine molecule, procaine amide, dis-

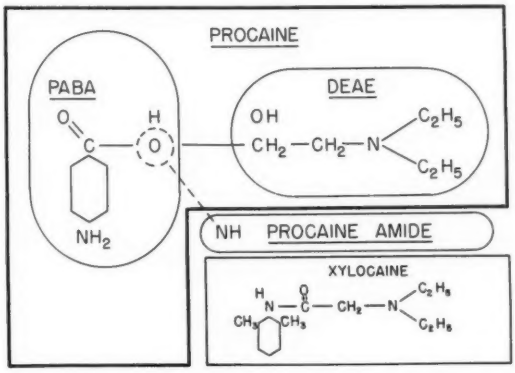

FIG. 7. These diagrammatic representations indicate chemical structures of various substances injected. Moieties (enclosed by fine lines) of the procaine molecule (enclosed by heavy line) are para-aminobenzoic acid (PABA) and diethyl-aminoethanol (DEAE).

played no capacity whatever to inhibit seizures. The drug was tested on two occasions, the lack of effect being confirmed by demonstrating complete protection upon a subsequent administration of procaine (Fig. 6). The injection of procaine amide caused little change in the electroencephalographic record except a slight synchrony after 10–20 ml. (25–30 mg./kg.) had been given although, concurrently, the electrocardiogram was markedly abnormal. Even after such large dosages, the animals appeared only slightly "dopey" for a very short time (Fig. 5).

In order to explore further the chemical elements responsible for protection against seizures, by procaine, it was decided to test the effect of ad-

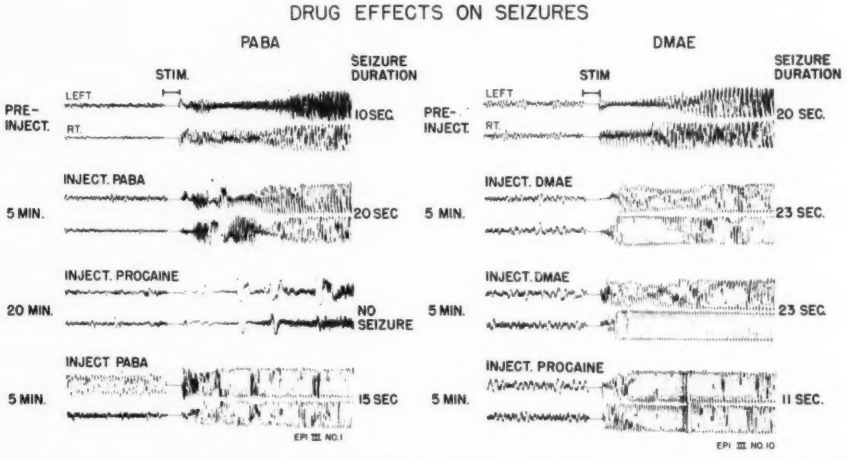

FIG. 8. Neither para-aminobenzoic acid (PABA, left column) nor dimethylamino acid (DMAE, right column) afforded any protection against seizures, as indicated by these tracings. Subsequent injections of procaine were effective following failure of PABA to inhibit convulsions but not following injection of DMAE.

ministration of each of the two procaine moieties (or a similar substance), para-aminobenzoic acid and diethyl-aminoethanol (Figs. 7 and 8). Because the latter chemical was not available, its effect will be examined later, but a closely related substance, dimethyl aminoethanol, was investigated. Neither of these agents induced any significant change in the electroencephalogram or in the behavior of the animal even when as much as 20 ml. (25–30 mg./kg.) were injected. Similarly, neither inhibited induction of seizures. In fact, dimethylaminoethanol seemed to prevent protection by procaine, as injection of the latter substance in an animal that had been tested with the former afforded only partial protection from the induced convulsive manifestations (Fig. 8).

DISCUSSION

The anticonvulsant properties of procaine were first reported in the physiological literature by Bernhard and Bohm[1] in 1954, although these

authors referred to somewhat similar results in rats described by Mercier in 1950.[9,10] Later, the observation was confirmed by Yasukata,[14] and extended by the Swedish authors[2] and by Tanaka in this country.[13] Bernhard and Bohm elicited seizures by cortical stimulation of curarized cats and monkeys which had received, additionally, small amounts of barbiturates, and found tetracaine to be the most effective agent in blocking seizures. As it also proved to be the most toxic, they concluded that lidocaine (Xylocaine) was the most satisfactory preparation for experimental use. Tanaka tested the relative capacity of a variety of procaine-like drugs to protect rats from convulsions elicited by electroshock and by Metrazol injections. He found that procaine, cocaine, and Trasentine (adiphenine) possessed anticonvulsant properties but indicated that cocaine was considerably more toxic than the other substances.

The results of the experiments reported here agree in general with those described above. It is clearly evident that intravenous procaine is capable of blocking convulsive activity completely for a short time in animals. However, we found procaine to be more effective and less toxic than Xylocaine in unanesthetized monkeys, and hence must conclude that the synergistic effect of barbiturates contributed importantly to results obtained by Bernhard and Bohm. These authors recognized this synergism but correctly pointed out that the amounts of barbiturates used by them was far too small to block seizures by its own action.

While observations are still fragmentary, evidence exists that indicates that the seizure-blocking effects noted above apply to man as well as to experimental animals. Bernhard and Bohm[1,3] have reported their experiences with the use of intravenous Xylocaine in terminating prolonged seizure manifestations and in the treatment of status epilepticus. Additionally, Ottosson[12] has markedly shortened the ictal phenomena associated with electroshock therapy by prior administration of Xylocaine. It is notable, perhaps, that his patients also received "light Evipan anesthesia" as well as succinylcholine iodide, but the use of these substances was well controlled in the study.

The nature of accumulated evidence indicates that protective effects afforded are fleeting and that they require the presence of a high concentration of circulating procaine. While, as indicated, relatively large amounts of the drug are being injected currently for other disorders, administration is usually accomplished by slow intravenous drip for prolonged periods of time; such dosages, in all probability, while beneficial, are insufficient to induce blockade of seizures. Rather, it seems likely that relatively large amounts of drug must be injected rapidly if interruption of convulsive activity is to be achieved. Presently existing concepts concerning the hazards involved in such therapy, therefore, dictate that extreme caution must be exerted in exploring the problem clinically.

We have been able to make, so far, but a single clinical observation regarding the use and effects of intravenous procaine in convulsive disorders.

Our patient was a 31-year-old man with thrombo-angiitis obliterans, comatose and in status epilepticus, who was considered to be in the terminal stages of the disorder because of intracranial involvement. In the course of less than an hour, he was given three injections, each consisting of 10 ml. of 1 per cent procaine (1.7 mg./kg.), and one of 20 ml. of 1 per cent procaine (3.4 mg./kg.), in each instance at the rate of 10 ml. per minute. Following each injection, the seizures temporarily abated or ceased and the appearance of the patient improved, but such effects were exceedingly evanescent. Subsequently, procaine therapy was discontinued, and general supportive measures were reinstated. Because of other drugs and therapies being concurrently given to this critically and presumably hopelessly ill man, his rapid and complete return to alert consciousness in 8 hours and, subsequently, to recovery can in no way be assigned exclusively, or perhaps at all, to the procaine medication. The coincidence, however, if it was such, was highly gratifying, and the observations concerning the transient beneficial effects upon the seizures exerted by the drug seem valid.

There is no clear-cut evidence to indicate the optimum dosage required to induce blockade of seizures or the degree of safety with which procaine can be administered. Bernhard and Bohm, in their animal experiments, employed relatively small dosages (1.0–2.0 mg./kg.) of Xylocaine in conjunction with a barbiturate (and the synergistic properties displayed would suggest that a barbiturate would be a valuable adjunct to employ with whatever procaine-like substance was used clinically). In their patients, they supplemented a continuous Xylocaine drip with repeated rapid injections of as high as 6.0 mg./kg. of Xylocaine,[3] while Ottosson's[12] patients were given 2.0–4.0 mg./kg. of the drug. Our patient received about 3.5 mg./kg. of procaine in a single dose although here, perhaps, it is pertinent again to point out that, as a local anesthetic, Xylocaine is said to have twice the potency of procaine for equal concentrations. Certainly, any clinical investigations employing such agents must be attended by the utmost caution until further data regarding their use become available.

There is as yet little evidence to indicate the manner in which procaine-like substances protect against seizures. It has been pointed out that the action of these agents as local anesthetics cannot account in itself for their capacity to inhibit seizures, as many local anesthetics do not display this property.[2] Certainly, the effect is mediated by cerebro-central rather than spinal mechanisms. Bernhard and Bohm have shown that "Lidocaine, in doses which abolish the experimental epileptic fit, has no significant effect on the spinal reflexes; the monosynaptic and polysynaptic reflexes may be reduced only to 70–90% of the pre-injection values."[2] Their studies indicate, moreover, that lidocaine abolishes the cortically evoked facilitatory effect upon spinal motor neurons yet does not influence potentials evoked in sensory area II by peripheral excitation.

For reasons stated above and for others to be advanced, it is highly probable that the anti-epileptic action of these substances may be assigned to an effect upon mechanisms mediated by the central cephalic brain stem.

This region, equivalently involved in caudally oriented facilitation and inhibition upon spinal motor activity,[8] and in cephalically directed processes underlying maintenance of the alert state,[11] is clearly rendered functionally disordered by diffuse convulsions.[6] Evidence has been adduced, indeed, that indicates that diffuse convulsions cannot be sustained if conduction activity in the central cephalic brain stem is blocked by destructive lesions[4,5] and it is likely that the anticonvulsive effects of soporific drugs depend in large part upon their selective action in this region. The observations reported here, however, would suggest that inhibition of seizures is not necessarily a function of the sedative effects known to be a property of other drugs employed in epilepsy. Certainly, our animals, after an initial and very transient period, exhibited neither behavioral nor electroencephalographic evidence of cerebral depression during the time of blockade of seizures. Moreover, there is information to indicate that conductive phenomena in the reticular formation may be modified by drugs without the induction of electroencephalographic synchrony or of cerebral depression.[7] It can only be postulated that the agents effective in seizure-inhibition described here may act upon this region in a similar selective manner.

The basic structure of the chemical molecule common to agents tested thus far that exhibit this type of anti-epileptic property can only be surmized. Tanaka has indicated that "All compounds tested, the chemical structure of which contains a dialkylaminoalkyl linked via O, N or C to an aryl or aralkyl radical, were found to exhibit anticonvulsant activity."[13] This concept would appear to be not entirely satisfactory, as procaine amide tested by us displayed no protective qualities whatever. Obviously, extensive further investigation will be required to resolve the problem.

Because the action of these drugs described is so fleeting, one can question, with some justification, the clinical importance of the observations. While no direct benefits to the epileptic problem can be predicted with confidence, certain possibilities, at least, exist. The effect exhibited by procaine-like agents in inhibiting seizures without depressing cerebral activity would seem to be a highly desirable feature to be further explored. To achieve widespread clinical usefulness, a search must be made either for similar drugs that afford protection of longer duration, or for a means of making available, perhaps from depot sources, higher concentrations of agents described for longer periods of time. Of these possibilities, the former would seem to be the more fruitfully investigated. Possibly of more immediate value, would be tests directed at the actions of these agents in reversing status epilepticus or in influencing therapy for mental disorders, either through modification of the seizure component of electroshock therapy or otherwise. In any event, the phenomenon described is a highly intriguing one, worthy of scrutiny if for no other reason than that it may yield insight into studies of physiological functions of the brain.

SUMMARY

1. The intravenous injection of procaine hydrochloride was found to protect monkeys from seizures initiated by direct cortical stimulation and

by a technique identical with the use of clinical electroshock therapy. This protective capacity, tested in 10 animals, persisted for approximately 30 minutes and did not require the induction of a persistent state of cerebral depression in the subjects.

2. Of other agents tested, similar in structure to procaine or to its moieties, only Xylocaine afforded similar protection, to a lesser degree.

3. The results of rapid intravenous injections of procaine in a patient in status epilepticus are described.

4. The possible mode of action of the agents employed and potential clinical application of the phenomenon are discussed.

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VARIATIONS IN THE SPINOTHALAMIC TRACT IN MAN*

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THIS is a report of two cases that illustrate the variability of the pain pathways in the spinal cord of some individuals.

Standard textbooks of neuroanatomy[3,5,6] give descriptions and present diagrams indicating that the pain pathway in the spinal cord in man is a discrete bundle of fibers, known as the spinothalamic tract, located in the anterolateral funiculus and consisting of afferent neurons of the second order. Finely myelinated or unmyelinated dorsal root fibers that serve as pain conductors terminate in the gray matter almost at once after entering the cord. From cells in the posterior column of the gray matter fibers arise which, in man, cross to the opposite side of the cord in the anterior white commissure and ascend in the lateral spinothalamic tract to end in the thalamus. Unilateral section of this tract produces complete loss of pain and temperature sensations on the opposite side of the body, extending upward to a level one segment below the level of the lesion, because of the oblique crossing of the spinothalamic fibers.

These and similar statements are the result of piecing together fragmentary bits of clinical and experimental facts obtained over a period of many years. Unfortunately, our knowledge of the pain pathways in the spinal cord is still far from exact and the dogmatic statements and diagrams to be found in most textbooks cannot be substantiated by clinical observations. White and Sweet[9] in their extensive monograph on pain have reviewed the knowledge accumulated to date on the pain pathways in man.

CASE REPORTS

Case 1. Mrs. L.K. was the subject of a brief report before the Chicago Neurological Society 6 years ago. This was published in abstract form a year later.[8] During the course of a left unilateral anterolateral cordotomy on a 46-year-old white woman with intractable pain of the right lower extremity, it was discovered that there was analgesia to pin prick below the umbilicus on the left although there was no demonstrable sensory loss on the right side. Thirty-eight days later right unilateral anterolateral cordotomy was carried out and was eventually extended to section of the right anterior quadrant of the cord. This produced analgesia to pin prick between the umbilicus and the anterior aspect of the knee on the right (T11 to L2 dermatomes), with preservation of pain sensation in the lower lumbar and sacral dermatomes. The analgesia on the right later receded to hypesthesia but the

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analgesia on the left was maintained at the level of the umbilicus up to the time of dismissal from the hospital, 103 days after the section on the left and 65 days after the cordotomy on the right. She died at home 2 years later. No necropsy was obtained.

Case 2. Mrs. A.P. was a 51-year-old white woman who had had pain in the right lower extremity for 9 months, caused by recurrent adenocarcinoma of the uterus. High thoracic left anterolateral cordotomy was carried out without incidence under local anesthesia. A sensory level between the costal margin and the nipple (T6 dermatome) was obtained. The patient was relieved of her pain in the right lower extremity and left the hospital 11 days after operation.

Five months later the pain had returned with its former severity. There was loss

FIG. 1. Photomicrograph of cross-section of spinal cord at T1 segment (fat stain).

of sensation to pin prick to the level of the costal margin (T8 dermatome). Careful examination failed to reveal any "islands" of sensation below this level.

The patient continued to complain of the pain in the right lower extremity. There was no change in her sensory level. Thirteen months after the first cordotomy the previous incision was reopened and the previous laminectomy was extended to include the next lowest vertebra. Then right anterolateral cordotomy was carried out, making an incision 5 mm. deep anterior to the dentate ligament and extending medially to the anterior roots. A level of anesthesia to pin prick below the costal margin on the left was obtained. This level receded in 10 days to the level of the umbilicus (T10 dermatome). The patient was relieved of the pain in her right lower extremity and left the hospital 13 days later.

She was readmitted 2 months later and died 72 hours after admission, 15 months after unilateral cordotomy and 69 days after right unilateral cordotomy. The spinal cord was removed 4 hours after death and fixed in formalin.

Later examination revealed that the specimen extended from T1 segment to the conus medullaris. There was superficial damage to the left side of the cord at T3 and T4 segments. This was apparently caused by dural adhesions at this point. This area included the left anterolateral cordotomy incision. The right cordotomy incision was readily identified in the T5 segment. Fig. 1 is a microphotograph of a fat stain of a cross-section of the 1st thoracic segment. Degeneration in the periphery of the left anterolateral funiculus is easily noted. On the right there is similar but less marked evidence of degeneration.

Case 1 is unique. The only other case found in the literature is that of French and Peyton.[1] They carried out a cordotomy on the right side at the 3rd thoracic level because of pain in the left groin and lower extremity. This gave loss of pain and temperature sensations below the 6th thoracic dermatome on the right. Later cordotomy was carried out on the left at the 4th thoracic segment, with loss of pain and temperature sensations below the 8th thoracic dermatome on that side. Unfortunately, necropsy was not obtained in either of these cases. French and Peyton postulated a diplegia of the spinal cord at the lumbar or lower thoracic level in their patient. In Case 1 presented above, the unusual distribution of the anesthesia on the right side, with loss of sensation on the lower ipsilateral trunk and upper anterior thigh, and retention of sensation in the lower lumbar and sacral dermatomes on the right side, suggests a reversal of the normal lamellation of the spinothalamic tract in this patient.

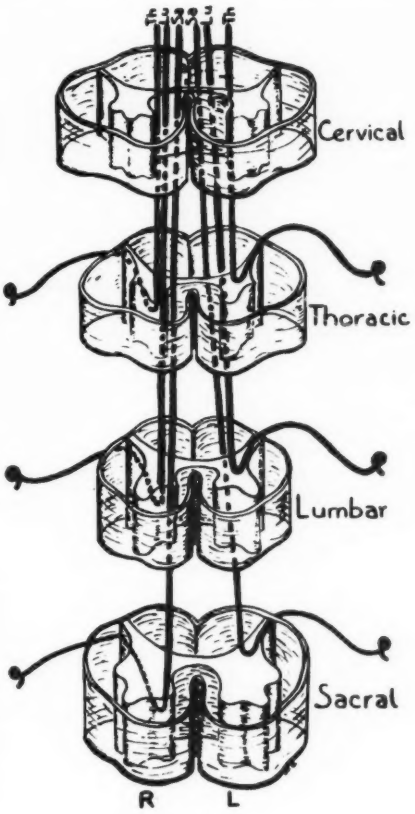

FIG. 2. Diagram showing, on right, a hypothetical possible grouping of the uncrossed pain fibers in the spinal cord of Case 1, and, on left, the accepted grouping of fibers of the dorsal funiculus.

Petrén[4] thought that the ascending pain fibers in the spinothalamic tract gradually shifted lateralward as they ascended. This has been verified by many observers. It is likely that this lateral shift is caused by displacement by the decussating sensory neurones of the second order, since these apparently turn rostad after crossing the midline. On the other hand, uncrossed ascending sensory neurons might be expected to group themselves so that the caudal fibers are

deepest and the fibers from higher levels are more superficial. This type of grouping is seen in the dorsal funiculus of the cervical spinal cord where the fasciculus gracilis contains uncrossed afferent fibers from the lower extremity (sacral and lumbar segments) and the more lateral fasciculus cuneatus contains afferent fibers from the upper limbs. Fig. 2 is a diagram illustrating a hypothetical grouping of the afferent uncrossed pain fibers in the right side of the spinal cord of Mrs. L. K. (Case 1) with the lower lumbar and sacral fibers close to the midline in the anterior quadrant of the thoracic and cervical spinal cord. It is also possible that the uncrossed pain fibers in the right side of the spinal cord of this patient remained in the dorsal region near the dorsal gray matter, or at least posterior to the plane of the dentate ligament where they would have escaped the cordotomy incision.

Sweet and his associates[7] stimulated with electrodes lying within the anterior half of the spinal cord and reported that 17 per cent of 187 such stimulations yielded pain referred ipsilaterally (11 per cent) or bilaterally (6 per cent). However, the possibility of spread of current to the contralateral anterior funiculus in these stimulations suggests itself.

White and Sweet[9] described a patient who had an initial cordotomy on the right at the 3rd thoracic segment, with analgesia up to the 7th rib on the left, except for the left anoperineal region and medial buttock, where there was hypalgesia. Pain persisted in this area. Another right cordotomy at the 2nd thoracic segment did not alter the sacral island of hypalgesia or relieve the pain. A third cordotomy on the left at the 1st thoracic segment produced analgesia on the right below the 4th rib; the sacral segments on the left were analgesic as well and the patient was free of pain below his waist until his death 5 months later.

Case 2 substantiates these observations of White and Sweet. However, Mrs. A. P. had no demonstrable islands of sensation to pain below her level of analgesia at the 6th thoracic dermatome. This proved to be true on repeated sensory examinations during the 13 months between her two operations. After ipsilateral cordotomy her pain was relieved.

Kahn[2] and White and Sweet[9] have emphasized that cordotomies for pain must extend posteriorly to the plane of the dentate ligament in order to eliminate pain responses over the buttock and the lateral aspect of the hip. I have verified this on several occasions while carrying out cordotomy under local anesthesia. However, there are individual variations, at times even in the same patient. The following case is an example.

Case 3. Rev. E.O., a 40-year-old priest, had bilateral two-stage anterolateral cordotomy for persistent bilateral sciatic pain which had followed five lumbar laminectomies performed elsewhere for multiple lumbar disc protrusions and arachnoiditis of the cauda equina. At the first stage, cordotomy was carried out on the left side at the level of the 5th thoracic vertebra. After a level of analgesia at the level of the right costal margin had been obtained, there was still an island of sensation to pain over the right buttock. This disappeared when the incision was extended posteriorly to include the plane of the dentate ligament.

Two weeks later cordotomy was carried out on the right side at the level of the 4th thoracic vertebra. An incision 5 mm. deep was made beginning just anterior to the dentate ligament and extending just anterior to the ventral root. This produced analgesia to the left costal margin with the exception of an island of sensation over the left buttock, extending up to the iliac crest. Then the incision was extended posteriorly to the plane of the dentate ligament. This produced analgesia to the level of the 6th rib anteriorly but did not ablate the island of sensation on the right buttock. When the incision was deepened medially to a depth of 6 mm. there was analgesia to pain everywhere on the left below the 6th rib.

Thus in this patient the sacral fibers for the right buttock appeared to be located posteriorly in the left anterolateral funiculus at or near the plane of the dentate ligament. The corresponding fibers for the left buttock lay deeper near the midline on the right and medial to the emergence of the anterior root.

As Kahn[2] and White and Sweet[9] state, cordotomy incisions must be at least 5 mm. deep and must extend to beyond the emergence of the anterior roots. While they must not extend to the midline and wound the anterior spinal artery, it is essential that the anterior quadrant of the spinal cord be as nearly completely sectioned as possible. Kahn[2] stated categorically that an incision 4 to 5 mm. in depth, that starts at the attachment of the dentate ligament and extends to 2 mm. anterior to the anterior nerve root, will produce high levels of analgesia that rarely fall. His experience seems to be largely with high cervical cordotomies. My experience parallels more closely that of White and Sweet,[9] who have found it necessary to make deeper and more medial incisions in some cases, often approximating a complete anterior quadrant section. White and Sweet[9] appear to have carried out usually high thoracic cordotomy. Almost all of my cordotomies have been at the high thoracic level.

CONCLUSION

If pain persists after an adequate cordotomy at an appropriate level, repeated meticulous sensory examinations must be carried out. If any regression of the level of analgesia occurs or if islands of pain perception, especially in lumbar or sacral dermatomes, appear, the wound should be reopened and the incisions in the anterior quadrants should be deepened. The surgeon should be certain that the incision extends dorsally to the plane of the dentate ligament and medially for 2 or 3 mm. medial to the emergence of the anterior roots. In cases of persistent unilateral pain after an adequate contralateral cordotomy, ipsilateral cordotomy should be considered. As White and Sweet[9] suggested, bipolar stimulation of the ipsilateral (to the pain) anterior quadrant of the cord under local anesthesia may help to indicate an ipsilateral cordotomy.

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THE THORACIC HERNIATED INTERVERTEBRAL DISC SYNDROME

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SINCE large series of herniated thoracic discs have not been reported, the present group is being tabulated in some detail. For the reason that 2 of the cases present unusual findings that, to our knowledge, have not been reported elsewhere, we have felt this group would be of interest.

In the Albany Hospital in the last 15 years, 10 herniated intervertebral discs in the thoracic region have been confirmed at operation. These appeared in a series of 2,026 cases in which the diagnosis of herniated disc was made. In 1,145 cases this was confirmed at operation. The others were cases in which the patients received conservative treatment and which were therefore unverified. This is about five times the incidence (12 in 5,500 cases) reported by Love and Kiefer in 1950.[7] Of this series of herniated thoracic intervertebral discs, the location and chief presenting signs are recorded in Table 1. Roentgenological findings and cerebrospinal fluid changes are listed in Table 2.

The two cases described below make it clear that, while progressive pyramidal tract signs usually appear, preceded by radicular pain at the level of the herniation, this is not necessarily the case. A variety of misleading neurologic signs are to be anticipated. A single, well-defined syndrome, such as one sees with the herniation of a cervical disc or a lumbar disc, is not the rule. In only 3 of the 10 cases tabulated was a diagnosis of herniated thoracic intervertebral disc seriously entertained from the clinical examination, roentgenologic findings and cerebrospinal fluid protein level. Even radicular pain at the level of the lesion is not frequent. When present it is not characteristically intermittent as is the pain associated with other discs, and it may even disappear after a time. This peculiarity of the pain, coupled with slowly progressive signs of cord involvement, often leads to a diagnosis of cord tumor.

In 1 case the plain roentgenograms revealed narrowing at the interspace where the herniated disc was ultimately demonstrated. In 4 cases myelography showed a complete block at or within 1 cm. of the interspace involved, and in 6 cases a partial block was found laterally placed and usually centered over the interspace at which the herniation had occurred. The range of the cerebrospinal fluid protein was 31 mg. per cent to 194 mg. per cent, with an average level of 92.4 per cent.

* Deceased February 15, 1956.

TABLE 1

Location and chief presenting signs of herniated thoracic intervertebral discs

Case and Hospital No.	Location	Presenting Signs	Duration of Symptoms	History and Onset	Age	Sex	Occupation
1. J.P. A42332	Right T8–9	Right, then left lower chest pain. Complete paraplegia, incontinence. Ill-defined sensory level of short duration just before operation	5 wks.	No trauma. Gradual onset. Paraplegic 3 wks.	56	F	Housewife
2. R.B. A56112	Left T9–10	Hyperreflexia, marked mid-dorsal pain, vibration over sacrum absent	4 mos.	No trauma. Gradual onset low back pain	48	M	Policeman
3. S.L. A4725	Midline T9–10	Spasticity in lower limbs. No sensory changes	5 yrs.	No trauma (other than asthma). Gradual left leg weakness	41	M	Pharmacist
4. L.S. A85775	Left T11–12	Weakness, hyperactive reflexes. No sensory signs	6 mos.	No trauma. Gradual onset leg weakness	42	F	Pocket setter
5. H.M. A35537	Left T11–12	Hyperactive reflexes, position sense absent in right great toe, vibratory sense absent below L1 level	5 yrs.	No trauma. Gradual onset intermittent low back pain	43	F	Bookkeeper
6. H.S. B82077	Left T11–12	Hyperreflexia, no weakness. Predominant signs loss of position sense in legs	1 yr.	No trauma. Sudden onset low midline backache	36	F	Housewife
7. J.B. A59336	Right T11–12	Local back pain, no sensory changes, no pyramidal tract signs	3 mos.	No trauma. Sudden onset pain middle of back while "toggling leather"	36	M	Leather worker
8. K.H. 94667	Midline T11–12	Pyramidal tract signs, no sensory signs	4 wks.	Fell on ice and injured back 4 mos. before onset. Sudden onset dull lower lumbar pain 4 wks. before admission	27	M	Photographer
9. M.G. A97994	Midline T11–12	Weakness, hyperreflexia, very vague sensory level below T12	2 days	Lifting egg crates. Sudden onset pain middle of back (2 yrs. before onset pain left leg, cleared up 1 yr. before admission)	18	F	Dairy manager
10. C.P. B87439	Midline T12–L1	Weakness lower limbs without pyramidal tract signs, absent ankle jerks. No sensory signs. Some right hip pain	1½ yrs.	No trauma. Gradual onset right hip pain and weakness 1½ yrs. before admission. Sudden onset bilateral leg weakness 2 mos. before admission after airplane ride	68	M	Retired office worker

The following case histories are presented as unusual variations of herniated intervertebral disc syndromes in the thoracic region.

CASE REPORTS

Case 9. M.G. (A97994), a 20-year-old white single female, was admitted to the Albany Hospital by way of the emergency room on July 4, 1951 with the chief complaint of pain in the back and legs. Two years earlier she had had pain in the left leg and was uncomfortable when sitting, without history of back injury. This had lasted about a year and then cleared up.

The day before admission the patient was lifting cases of eggs and butter weigh-

TABLE 2

Roentgenologic findings and cerebrospinal fluid changes in cases of herniated thoracic intervertebral discs

Case and Hospital No.	CSF Protein mg.%	Plain X-rays	Myelogram
1. J.P. A42332	78	None taken	Partial block at level of interspace
2. R.B. A56112	80	Diffuse bridging and spurring dorsal spine	Partial block at level of interspace
3. S.L. A4725	31	Cervical taken only	Complete block at level of interspace
4. L.S. A85775	99	Negative	Complete block at level of interspace
5. H.M. A35537	70	None taken	Partial block at level of interspace
6. H.S. B82077	118	Diffuse spurring dorsal spine	Partial block not centered at level of interspace
7. J.B. A59336	52	Cervical taken only	Partial block at level of interspace
8. K.H. 94667	107	Narrowing D10–11 (disc found at D11–12)	Complete block at level of interspace
9. M.G. A97994	194	Narrowing at level of disc (D11–12)	Complete block at interspace
10. C.P. B87439	95	Diffuse hypertrophic changes dorsal spine	Partial block at interspace

ing between 30 and 50 pounds. She began to have pain over the sacrum. By night this had radiated to the anterior aspect of both thighs down to the instep of both feet. Coughing hurt her. About noon of the day of admission it became excruciating. She was given 8 mg. of morphine without any effect. About 1:00 P.M. she was admitted to the emergency room in extreme discomfort. There had been no difficulty with bladder or bowel.

Examination. The patient was writhing in pain. She could not stand, but one could not be sure whether this was because of pain or weakness. In the prone position, there was mild spasm of the paravertebral muscles. Recumbent, there was moderate spasm of the abdominal wall on the right without tenderness. Straight leg raising was 20° on the right and 30° on the left. Generally, muscle strength could not be tested because of guarding, but the rectal sphincter was extremely relaxed. The right lower abdominal reflex and the right knee jerk were diminished. There was diminished perception of pin-prick below T12 except for bilateral hyperalgesia in the L5 dermatomes.

Myelography, performed after roentgenograms had showed some narrowing of the T11–12 interspace and posterior spurring at that level, revealed a complete

block at the level of the body of T12. Queckenstedt test produced a slow rise to 350 mm. of cerebrospinal fluid with no fall. Cerebrospinal fluid protein was 194 mg. per cent.

Operation. Immediately after myelography, laminectomy was performed at T10, 11, 12, and L1. The cord was found to be humped backwards. An incision in the posterior column on the right, where the posterior displacement was greatest, revealed a small hematoma in the cord, which was less than 1 cc. in volume. A small biopsy from the wall of this hematoma was reported to show some proliferation of ependymal cells which might represent part of an ependymoma. The cord, however, did not return to its normal contour. After exploration anterior to the cord intradurally had been inconclusive, extradural search revealed a soft midline protruded disc at the T11–12 level. This was removed and the wound was closed with interrupted black silk sutures.

Pathologic Report. The fragments from the disc were reported to show focally degenerated fibrocartilage.

Course. The patient had an uneventful recovery and was discharged from the hospital with bilateral foot drop and considerable weakness of the legs. Postoperative cystometrogram revealed a normally functioning bladder.

She has been followed now for some 4 years and still has a moderate bilateral foot drop and hyperactive deep tendon reflexes. However, she is able to walk fairly well without crutches and has been able to work. There has been no progression of her signs since the operation.

Comment. It seems highly unlikely that the pathological findings in the wall of the small hematomyelic cavity represented an ependymal neoplasm. On careful re-examination of these slides, one small area was found in which it was thought an ependymoma could be clearly demonstrated. If this proves to be true, it appears probable that the disc herniation produced a hematoma in a very small ependymoma by direct trauma.

Case 6. Mrs. H.S. (B82077), referred by Dr. Snyder of Corinth, New York, was seen first in an office examination on Dec. 20, 1954, at which time she complained chiefly of inability to use her legs properly. About 1 year earlier, severe backache began to develop in the lower thoracic region, which occasionally radiated into the lower abdomen, of variable intensity, but usually worse about 3 or 4 o'clock in the morning. As time went on, her pain did not change a great deal until 6 months prior to examination, when tingling began to develop in her feet and the pain ceased. Within 2 or 3 months this tingling was replaced by gradually increasing numbness, from the lower abdominal region downward. By this time her feet had become numb so that she was unable to walk with her eyes closed. She had not noticed any weakness in the legs, any disturbance of bladder or bowel, nor any loss of weight.

Examination at that time revealed a positive Romberg with complete loss of position sense in the lower extremities. Knee and ankle jerks were very lively, with variable, unsustained patellar clonus and normal plantar reflexes. There was slight hypalgesia bilaterally in the T11 dermatome. Relaxation of the lower abdominal musculature was evident, producing a pronounced "pot-belly," to a greater degree than in the average female of her age.

She was admitted to the hospital on Jan. 2, 1955, the delay occasioned by personal reasons.

Examination. On admission there was hypalgesia from the T11 level downward,

together with positive Babinski signs, sustained ankle clonus, hyperactive knee and ankle jerks, but no weakness in the lower limbs and no difficulty with bladder or rectum. The lower abdominal reflexes were depressed. The most severe impairment noted in her neurologic examination was complete loss of position sense in her legs. Straight leg raising could be carried to 30° on the right and 90° on the left.

Myelography revealed a partial block at the level of T11. Cerebrospinal fluid protein was 118 mg. per cent. A preoperative cystometrogram disclosed a mildly hypotonic bladder.

Operation. Intradural extra-arachnoid exploration demonstrated a long, low, flat mass anteriorly, lying extradurally. The dura mater was closed and the mass was removed. It was a large, partially calcified herniated intervertebral disc at the T11–12 interspace.

Course. The patient had a somewhat more hypotonic bladder postoperatively, as demonstrated by a cystometrogram done immediately after operation, but within 1 week this had returned almost to normal and she was voiding without residual.

DISCUSSION

The incidence of thoracic disc protrusion varies widely. Mixter and Barr[9] reported 1 thoracic protrusion among 19 cases of herniated disc. The report of Hawk[5] indicates a rather high incidence of thoracic protrusion. Love and Walsh[8] reported 113 discs, of which 6 were thoracic. In 1950 Haley and Perry[4] reported complete autopsy on 99 spinal columns, and in 7 of this group there were multiple thoracic protrusions. These were autopsies picked at random, and the patients did not necessarily present symptoms during life. Svien and Karavitis[10] reported surgical treatment of a patient with such multiple protrusions in the upper thoracic region. In 1950 Love and Kiefer[7] reported an incidence of 12 in 5,500. They stated that no syndrome of intervertebral disc herniation in the thoracic region was found to be typical, as it was in the cervical and lumbar regions, and that of the total group of 17 herniated thoracic intervertebral discs collected from their own series and from the literature, in only 3 was the diagnosis made before operation. In 1952 Logue[6] reported 11 herniated thoracic discs in a series of 250. A group of 800 intervertebral discs operated on in the Montreal Neurological Institute revealed an incidence of 10 in the thoracic spine.[2] Epstein[3] made no attempt to determine frequency of thoracic disc disease because of so much variation in the available reports. Abbott and Retter[1] in 1956 reported that in a series of over 600 discs of all types, there were 11 protrusions in the thoracic region among 9 patients, and felt that the actual frequency was much higher than the incidence reported by Love and Kiefer. They also collected a total of 64 reported herniated thoracic discs in a careful review of the literature through 1955. This included their own series of 13.

As far as sex incidence is concerned, it was about equally divided in the Love and Kiefer[7] series, 9 females and 8 males. Abbott and Retter[1] were of the same opinion. In our own series there were 5 males and 5 females. However, these samples are so small that conclusions are not warranted, but it does appear that the distribution tends to be roughly equal in males and

females. Age distribution ranges from the young to the very old with the exception of the first decade.

Abbott and Retter[1] found 6 purely lateral protrusions in their group of 13 protrusions in 11 cases and stated that a fairly uniform syndrome was to be found in these patients as opposed to those with centrolateral protrusions. In our series, 6 of 10 protrusions were laterally placed and 4 were midline, but no such clear difference in the clinical picture was found between lateral and central discs. This may be ascribable to difference of definition, in that the 6 laterally placed discs might be considered centrolateral protrusions by other observers. It is worthy of note that 3 of our 10 patients had suffered from severe bronchial asthma for many years.

The first of the 2 unusual cases reported here presents an acute herniation of a thoracic disc with hematomyelia. After evacuation of the intramedullary hematoma and removal of the disc, the patient made a relatively good recovery. The interesting point in Case 2 is that the greatest neurologic defect was found in the posterior columns, with mild pyramidal tract involvement. From these findings it was anticipated that her lesion was causing pressure on the dorsum of the cord, which was the reverse of the actual situation.

To say the least, thoracic herniated discs present protean manifestations which can lead to incorrect diagnoses. Compression of the spinal cord appears to be much more frequent with herniation in the thoracic than in the cervical spine, so that early diagnosis and early removal of this compression is more imperative with a thoracic disc than with one in any other location. The urgency of early removal is made even greater by the fact that, whereas benign cord tumors produce slowly increasing compression with relatively good recovery following removal, the thoracic disc is subject to sudden additional herniation or extrusion subsequent to the onset of the disease. The sudden alterations in cord compression accompanying such protrusions result in the same lasting neurologic deficit commonly encountered in cases of spinal fracture and other rapidly developing compression of the cord.

Two depressing examples of such irreversible neurologic change have been observed by us. One of the patients in our Albany Hospital series remained paraplegic without any vestige of recovery for 3 months after operation, finally dying of intercurrent infection. The second patient was one observed on the Psychiatric and Urologic Services at various times. His T11–12 herniated disc had been removed elsewhere. Unimproved paraparesis was accompanied by excruciating pain in the lower limb. In spite of heroic efforts on the part of the patient to carry on a large general medical practice, he found himself increasingly disabled, first by the pain and then by the added burden of narcotic addiction. A unilateral prefrontal lobotomy was later performed at another hospital with little effect upon the pain and was followed by the subsequent development of postoperative epilepsy. Within 5 years after removal of the disc, this physician underwent complete dissolution of his personality and died.

SUMMARY

1. A series of 10 herniated thoracic intervertebral discs among 1,145 herniated discs confirmed at operation is reported.

2. Two cases which presented unusual findings are described in detail.

3. The previously recorded series are reviewed.

4. The conclusion is drawn that the only hope for such patients lies in early surgical intervention.

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A NOTE ON THE TREATMENT OF INVOLUNTARY MOVEMENTS OF THE ARM BY RESECTION OF THE BRACHIAL PLEXUS

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PARALYSIS agitans, chorea, hemiballism, and tremor resulting from birth palsies have been attacked surgically for more than 30 years. Various methods have been used and new ones are being devised. The many drugs introduced in recent years for control of such involuntary movements and rigidity have not, apparently, lessened the desirability for surgical treatment.

The patient whose treatment forms the basis of this report was seen many years ago before operations on the brain for athetosis and allied conditions could be performed with any degree of safety because of the lack of modern neurosurgical equipment, such as adequate suction and electrosurgery. Indeed, in these early years of neurosurgery even transcortical incisions of a relatively superficial nature were only rarely undertaken and the idea of an attack upon the basal ganglia could hardly have been entertained. We feel, therefore, that it would be of interest from the historical standpoint to present the case herein described, and it is also conceivable that even at the present time the treatment afforded this patient might in some instances be preferable to operations upon the brain.

HISTORICAL NOTE

In 1924 Hunter[13] advocated sympathetic ganglionectomy for the treatment of paralysis agitans, based on experimental evidence that sympathetic nerve supply to the muscle helps maintain its tonus. It is known that some surgeons attempted this, but the absence of reports in the literature attests to the negative results that must have been obtained.

In 1930 Pollock and Davis[17] reported a case of rigidity of an arm and leg as a result of paralysis agitans, treated by rhizotomy of the 4th cervical to the 4th thoracic posterior roots. The operation relieved rigidity of the arm temporarily, but the extremity went into contracture after operation and remained in that state.

In 1934 the first intracranial procedure was attempted for the relief of paralysis agitans by Delmas-Marsalet and van Bogaert.[11] It consisted of destruction of the dentate nucleus of the cerebellum. It was tried on only 1 patient. Rigidity was improved, but the tremor became worse and the patient died 10 days after operation.

In 1939 Bucy and Case,[7] following Horsley's work of 1909, reported one

case of extirpation of the precentral gyrus, an extrapyramidal suppressor area in the cerebral cortex. The "arm" area was removed. It was done in a case of right hemiparesis with coarse unilateral tremor. The operation resulted in partial paralysis. Tremor was abolished and had remained so at the time of the report, 15 months later.

This was followed by optimistic reports, including that of Klemme,[14] who used this method of treating dystonia, paralysis agitans, and athetosis in 100 cases. He stated the "results were amazing," carrying an operative mortality of 10 per cent, a very high rate of rehabilitation, and no recurrence of tremors relieved by this procedure within a 3-year postoperative period. It was pointed out by Bucy on later occasions[4,5] that considerable paralysis and increase in spasticity were produced by such extirpations, along with the desired loss of tremor.

A report by Bucy[6] in 1948 stated that all operations for treatment of involuntary movements thus far were distinctly experimental and that all were unsatisfactory in several ways. Cortical extirpations, he said, did not affect the progress of the disease, serious contralateral hemiparesis always resulted, and their indications were sharply limited to young patients with severe, nonprogressive unilateral disease.

In 1948 Browder[1] reported section of fibers of the anterior limb of the internal capsule in 15 patients with paralysis agitans, with beneficial results in 6.

Walker[19] reported a case of cerebral pedunculotomy for the relief of hemiballism in 1949. In this procedure one cerebral peduncle was cut across two-thirds to three-fourths of its lateral aspect, with excellent relief of tremor and rigidity, and an eventual sequela of slight weakness of the contralateral arm. We did not find further reports of this operation.

In 1949 Ebin[12] reported a new technique for relief of tremor of paralysis agitans, a combined lateral pyramidotomy with ventral pyramidal tract section on the opposite side by means of one oblique knife cut. In 1 case this was done bilaterally, with what was said to be a good result. This procedure was carried out also by Oliver[16] who reported in 1950 on 79 patients treated by section of the pyramidal tracts of the spinal cord, by this and other methods. In 19 of this group, the whole lateral column on one side was sectioned in the 2nd cervical segment. This seemed to be the most satisfactory type of pyramidotomy; only 1 patient was dissatisfied as a result. It gave almost complete relief of tremor, with slight homolateral weakness, slight contralateral weakness and contralateral hemithermoanesthesia the only final sequelae. There was no mention of relief of rigidity.

In 1950 Cobb and associates[8] reported a series of 9 cases of paralysis agitans treated by section of "U" fibers of the motor cortex, by an incision in Area 4, following Russell Meyers, who reported a good result in treating a case of hemiballism by this method. However, all 9 of Cobb's cases were failures.

Browder and associates[3] in 1953 reported a "capsular operation" in 2

cases of paralysis agitans, wherein the upper one-third of the head of the caudate nucleus was removed, followed by removal of the anterior capsule just rostral to the knee of the capsule to a depth of 7 to 8 mm. Reduction of rigidity and greater amplitude of the tremor were reported.

In 1954 Spiegel and Wycis[18] reported electrocoagulation of the ansa lenticularis in 6 cases of unilateral postencephalitic paralysis agitans. Tremor stopped almost completely in 2 cases. There was also some reduction of resistance to passive motion, but there were no sensory disturbances.

Cooper[9] reported 2 cases of surgical occlusion of the anterior choroidal artery, principally intended for patients with total incapacitation from unilateral paralysis agitans of long standing. Both patients improved considerably, 1 enough to work again, with much relief of rigidity and improvement in ability to speak. Two more such procedures were reported by Browder and Kaplan,[2] which resulted in moderate reduction of rigidity on the affected side and reduction of the rate of tremor by half.

In November 1955 Cooper and Poloukhine[10] reported treatment of paralysis agitans by destruction of the globus pallidus, using absolute alcohol, a "chemopallidectomy." Of 70 cases, they found immediate good results, consisting of abolition of contralateral tremor and rigidity without motor weakness, in 80 per cent, and lasting alleviation in 70 per cent of cases. This group is unique in that they included usage in senile and arteriosclerotic patients.

Narabayashi and associates[15] early in 1956 reported 26 cases of paralysis agitans treated by procaine oil injection of the globus pallidus. They stated that the principal symptoms of tremor, rigidity, and hyperhidrosis were relieved dramatically. Tremor tended to reappear after several weeks, but it was said that relief from rigidity was sustained. Complications included death in 1 case and supranuclear palsy in another.

One might conclude from the above that surgical treatment of spastic states and involuntary movements has not resolved itself into one highly effective, accepted procedure that has stood the test of time. It also seems, on the other hand, that enough progress has been made to justify continued efforts with intracranial operations.

REPORT OF A CASE

The patient was born in Russia in 1895. He did not remember ever having been well. He believed that he had large, suppurative lymph nodes or abscesses on the right side of his neck and face at the age of 2 or 3. He had several large, poorly healed scars on the right side of his neck and face, marking where, he believed, they were excised or drained. At the age of 5, he believed, a sudden right-sided paralysis developed, although he did not remember this event. He could not walk or talk. Gradually during the next month the paralysis began to clear up, that of the leg more completely than of the arm. The arm remained spastic and involuntary movements developed which became worse as the years passed. Athetoid movements of the right hand and arm were present fairly continuously, but a great increase of these movements was always initiated by any excitement, embarrassment, or other emotional upsurge. These movements were forceful and at times almost violent, and

of the usual purposeless type. At times, the patient said, the arm had done actual damage by knocking dishes from the tables in restaurants and homes before he could curb its motion with the left hand. Because of its continual movement and uncontrollable actions the arm was not only of no use to the patient, but was actually a hindrance. He was able to do all necessary things with his left hand.

The right foot had assumed the equinus position. This was improved by a plantar tenotomy in 1904.

In 1911, before the patient came under the care of the senior author, an incision was made below the right elbow and the ulnar nerve was injected with alcohol. No improvement was noted. In 1918 a biceps tenotomy was performed. This also brought no improvement.

On examination, in 1920, the right arm showed definite hypertrophy of all the muscle groups as compared to the left arm. The arm was usually held slightly everted and abducted, with the elbow slightly flexed (Fig. 1). The wrist and hand were extended, but the fingers were clenched tightly over the flexed thumb. The patient was unable to open the right hand except by forcing the fingers open with the left hand. From time to time the arm would be thrown into violent athetoid and uncontrollable movements, as described by the patient.

On May 28, 1920, at the suggestion of the late Dr. Harvey Cushing, the brachial plexus region was exposed and injected with 0.5 per cent procaine. This resulted in temporary anesthesia and loss of movement in the arm. This was done in order to paralyze the arm temporarily so that the patient could decide whether he would rather have a paralyzed arm or a strong but useless one with athetoid movements. Sensation reappeared within a few days, and with its return there was a throbbing, pumping pain down the right arm. He was advised to wait until this pain quieted down before resection of the plexus was attempted, but the pain continued. The patient decided that he wanted the brachial plexus resected.

On July 23, 1920, the patient entered Peter Bent Brigham Hospital. He complained of persistent pain in the right shoulder posteriorly. He had athetoid movements of the right upper extremity, accentuated by voluntary movements. He had hypertrophy of both right extremities. There was little voluntary movement of the right upper extremity and it was held in internal rotation.

On July 24, 1920, division and resection of the outer, inner and posterior cords of the right brachial plexus was carried out by one of us (G.H.) under local anesthesia, using 0.5 per cent procaine with epinephrine. Gaps of about $1\frac{1}{2}$ inches were left between the ends of the resected cords.

Following this operation a flexion contracture of the hand occurred, and some residue of athetosis of the fingers persisted, despite further exploration of the plexus region for aberrant nerves (Fig. 2).

On Aug. 6, 1920, division and resection of the median and ulnar nerves in the upper arms were performed, under procaine anesthesia. A 5-cm. segment of each of these nerves was removed in the region of the middle third of the biceps muscle. This obliterated the athetoid movements in the fingers.

On the first postoperative day it was found that the patient had complete paralysis of the right upper extremity except for small muscles of the thumb supplied by the radial nerve, the extensor and adductor pollicis. There was still some sensation in the thumb region. On discharge from the hospital on Aug. 14, 1920, the patient was "90 per cent satisfied." He could at that time extend the forearm a little if the arm was flexed at the elbow.

On Dec. 3, 1920, the patient returned on an outpatient basis because of athetoid

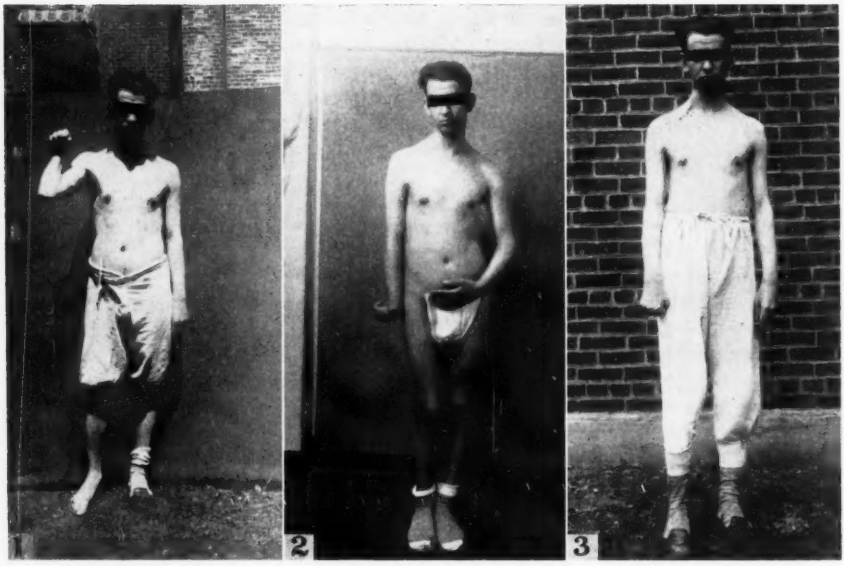

FIG. 1. Usual position of right arm. From this position it would make involuntary, purposeless, violent, uncontrollable movements. Hypertrophy of the upper arm is evident.

FIG. 2. After brachial plexus resection. The arm is paralyzed but the wrist is sharply flexed and has some athetoid movement.

FIG. 3. After resection of nerves in upper arm. The wrist is no longer flexed. There is now only slight athetoid movement in the thumb.

movements in the right thumb. The radial nerve was sectioned in the midforearm region. After this procedure, paralysis of the hand was complete (Fig. 3).

In December 1921, the patient's only complaint was a pulling sensation in the right shoulder. In September 1922, he noted some "shock-like" feelings through the right hand and heavy feelings in the fingers. He had a few blisters on the right hand from burns that resulted from lack of sensation. He reiterated that he was completely satisfied with the result of his operations.

In 1934 the patient had a subtotal thyroidectomy because of hyperthyroidism which had developed gradually during the preceding years. The last operation left him in a hypothyroid state and he has been taking thyroid extract daily ever since.

When seen in May 1956 the patient was still well satisfied with the condition of the right upper extremity, which was markedly atrophied and completely flaccid. Occasional fibrillary motions of the fingers occurred when at rest, but they did not bother him. His right lower extremity was very weak and the foot dragged during walking. There was a flexion contracture of the lateral four toes, and during the past several years painful, slow contractions of the plantar flexors of the right foot have been occurring several times a day with increasing frequency.

SUMMARY AND CONCLUSIONS

A review of surgical procedures used for the relief of involuntary movements and spasticity during the past 30 years is presented. Many proce-

dures attempted in the past have been discarded as useless or as producing too great a motor deficit, and of those employed most recently the follow-up period has not as yet been long enough to ascertain the end results.

A case is presented of unilateral severe athetosis of obscure origin, undoubtedly still progressive at its central lesion. In this patient the cords of the brachial plexus and peripheral nerves of the upper extremity were resected 36 years ago, leaving a flaccidly paralyzed extremity in exchange for a useless one dominated by very troublesome athetoid movements.

In the case presented, the patient remains well satisfied with the result of the paralysis of his arm in exchange for the uncontrollable, violent movement.

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FATAL BRAIN-STEM SHIFT FOLLOWING HEMISPHERECTOMY

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ALTHOUGH the first successful hemispherectomy was performed back in 1923 by Dandy,[14] who followed his first experience with a series of 6 cases, only recent advances in surgical technique, and perhaps a better understanding of neurophysiology, have made this operation the procedure of choice in certain cases of infantile hemiplegia[1,8,13,19,20,26–29,32–34,39,45] and a daring method for the so-called radical treatment of certain brain tumors.[2,4,14,24]

Since Krynauw[27–29] published his series, a large number of interesting reports, dealing with the uniformly satisfying results of this procedure, have invaded the literature. It was this powerful forward swing of the pendulum that prompted Mackay[31] to make a plea for some emphasis on contraindications and disadvantages, even failures, if these were encountered.

During the last 18 months, we have performed 5 hemispherectomies in patients with infantile hemiplegia. Three of them were clearly benefited by the operation and have been followed for 18 months, 15 months, and 11 months, respectively. They have shown marked improvement in their behaviour, definite relief of spasticity which facilitates rehabilitation procedures, and they are free of convulsions. The other 2 cases constitute the basis for this report because they presented a fatal complication which has not been reported in the literature reviewed by us and which, if interpreted correctly in this communication, calls attention to interesting points of intracranial dynamics.

CASE REPORTS

Case 1. *Left spastic infantile hemiplegia, epilepsy and temper tantrums in a young mental defective. Right hemispherectomy with profuse bleeding. Severe postoperative course. Brain-stem shift syndrome. No autopsy.*

History. A.E., male, 23 years old, was hospitalized at the Instituto Nacional de Enfermedades Neoplásicas on Nov. 28, 1954, complaining of generalized convulsions. He was the first child, of normal parents. The delivery was somewhat difficult, and he was born cyanotic and had difficulty in breathing for several minutes. When he was 4 months old, fever, generalized convulsions and a left hemiplegia developed. Since the age of 12 he had had crises which were preceded by a sensation of "emptiness" in the epigastrium and clouding of vision; then he became unconscious suddenly and had a grand mal seizure. He usually had two to three fits a month. He was quiet, humble, obedient, sociable, solicitous, affectionate and very attached to his mother, who cared for him devotedly because of his physical handicap. In

1953 his behaviour changed, possibly because of his stepfather's hostility, who was resentful because the boy did not work. The patient became irritable and developed temper tantrums. On one occasion he attacked his stepfather. He also became aggressive toward his brothers, quarreled with them frequently and expressed suicidal ideas.

Examination. He was a young man with a left spastic infantile hemiplegia. He was anxious, with a strong feeling of inferiority caused by his seizures and deformity. The mental tests (Wechsler-Bellevue scale) showed that he was a moderate mental defective. He had some insight and realized that he was excitable, anxious and irritable.

The electroencephalogram showed discharges of slow waves at the right frontal leads and in lesser degree at the left side with propagation to the parietotemporal leads. There were also many paroxysmal spike discharges in the right frontoparietotemporal leads. It was concluded that these signs were compatible with bilateral cortical atrophy, more marked on the right side. Plain roentgenograms of the skull showed no abnormalities. Pneumoencephalography (Fig. 1) revealed considerable dilatation of the right lateral ventricle with slight retraction which included the 3rd ventricle and left lateral ventricle. There were also signs of right cortical hemiatrophy. The cerebrospinal fluid pressure was 140 mm. of water. The fluid was clear and colourless, did not coagulate and contained 0 cells per c.mm.; protein was 36 mg. and chloride 780 mg. per cent; Pandy, Nonne, Kahn and cardiolipin reactions were negative.

Hemispherectomy. The patient was operated upon on May 5, 1955. A frontoparieto-occipital flap, divided in two portions, was raised. The dura mater was incised and after exposure of the hemisphere, the cerebral cortex was freed from adhesions. Because of the marked adhesions to the dura mater, the hemispherectomy had to be carried out by dividing the brain in four lobes. The hemostasis of the venous sinuses was very difficult, necessitating packing with oxycel and digital pressure. The basal ganglia were left intact. The dura mater was carefully closed and the bone flap was fixed by stainless steel wire. The right hemisphere was atrophied and was adherent to the dura mater in many places, specially at the level of the great veins. The patient tolerated the procedure well; it had lasted 8 hours and necessitated a transfusion of 4,300 cc. of whole blood to replace in part the blood that had been lost.

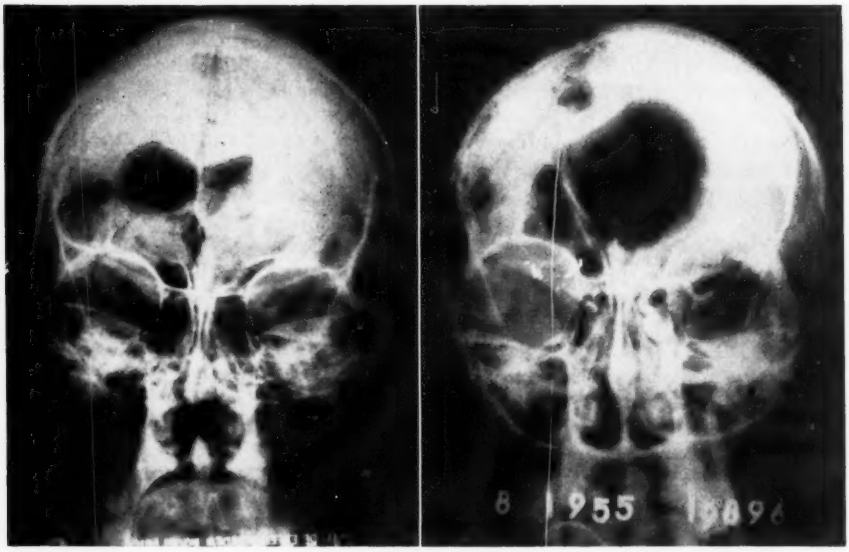
Postoperative Course. Immediately after the operation, periodic breathing developed and the patient was deeply unconscious for 28 hours. Gradually he recovered awareness but in an incomplete degree. Five days after the hemispherectomy he had his eyes widely open and spoke continually in a low unintelligible whisper while moving the right arm in all directions. He seemed grossly disoriented but when he heard the examiner sneezing he immediately said "God bless you, Doctor" in spite of the fact that he had not looked at him and did not seem aware of his presence. When asked how he felt he said, after 4 or 5 seconds, "a little better, Doctor" and answered that he complained of the head but could not specify what was wrong. In the same interview he would not answer other simple questions, which were put to him repeatedly; he closed his eyes and seemed to be asleep but several minutes later, when not interfered with, he recommenced the stereotyped movements of the right arm. The left hemiplegia was more marked but less spastic.

In the following days he was febrile, apathetic, uncommunicative. Gradually he partially recovered orientation in time and place, and 12 days after operation he

recognized the physicians and nurses. Slowly the hemiplegia improved to the point that he could move the arm and leg, but he could not walk again.

Forty-three days after operation the patient was still immobile most of the time, calm and silent. When addressed he would answer relevantly after about 15 seconds. If asked for the name of the month he took one minute to respond it was June. There was therefore marked retardation, the memory for past and recent events was deficient, and he was partially disoriented. The left hemiparesis was still very marked. He could move the arm and leg freely but could not walk or hold any objects in his hand.

Brain-Stem Shift Syndrome. On July 29, 1955 it was observed that the spasticity of the left limbs was much increased once more, and passive movements were very painful. He was very thin and doubly incontinent but seemed aware, ate normally and obeyed simple commands. Gradually the patient became worse. Considering the unfavourable course, arteriography and pneumoencephalography were done on Aug. 21, 1955, under general anesthesia. Up to that day the patient had continued deteriorating and was markedly retarded, immobile, mute, sleepy and indifferent. The pneumoencephalogram showed marked dilatation of the left lateral ventricle with the septum lucidum deviated to the right side (Fig. 2). The 3rd ventricle was also dilated and shifted to the right. The arteriogram demonstrated marked distortion of the anterior cerebral artery, which was partially located in the right side. After the contrast examinations the patient continued worse. He was indifferent, mute, made occasional movements of the right limbs, and he had a low-grade fever. He did not show any reaction to physical examinations, became comatose, and died on Sept. 15, 1955. No postmortem examination was permitted by the relatives.



FIGS. 1 and 2. *Case 1.* Pneumoencephalograms. (*Left*) Pre-operative. (*Right*) Postoperative. Notice marked shift of medial structures with displacement of the dilated left lateral ventricle towards the right side.

Case 2. *Right infantile hemiplegia in a girl with mental deficiency, epilepsy and severe behaviour problem. Hemispherectomy. Fairly good postoperative course. Brain-stem shift syndrome developed slowly 60 days after hemispherectomy. Postmortem confirmation.*

History. T.G., female, 23 years old, was admitted on Oct. 25, 1955 to the Instituto Nacional de Enfermedades Neoplásicas with the chief complaint of general convulsions since she was 20 months old. She was delivered normally and developed well until aged 2. At that time she had a grand mal seizure, fever and clouding of consciousness. When awareness was recovered she could not talk nor move the right limbs. During the next 6 months she had frequent tonic fits, of brief duration and without unconsciousness. She recovered speech progressively but continued to have localized convulsions until she was 7 years old. It was noted also that she had great difficulty in moving the limbs of the right side and they became stiff and deformed at the hand and foot. At age 7, the seizures became generalized; they were preceded by an undefinable aura, and were more marked on the right. After the seizure, she frequently became irritable and aggressive for several hours or days. Sometimes she had serial epilepsy, up to 25 crises a day. Generally she had about 20 attacks a month but after she was put on heavy anticonvulsive medication the seizures diminished to 2–4 a month.

She was very difficult at home, so she had to live alone with her mother. Her appetite was voracious. Sleep was variable; generally after the seizures she suffered from insomnia. The relatives reported that she was extremely irritable. Once she threw a heavy metal ash-tray at a 12-year-old nephew. The brother-in-law understood that she was a menace to the children and decided that she should live in another place. So she went to stay with her mother. There she behaved in a dominant way: would fix the hours for meals or for going to or getting out of bed. If her mother opposed any resistance she would push her violently, undress her and put her to bed by force. At other times she would lock her mother in her home and would not let her out for days. Her behaviour was, however, variable; some days she was calm and pleasant to everyone, other days she was "unendurable," excitable, aggressive, negativistic, filthy, and mean, and would go out untidy "to make the relatives ashamed" of her. The temper tantrums seemed to be worse every day. Once, she demonstrated affection and docility to an older sister, but later she became very hostile to her and one day she struck her fiercely. Very frequently she precipitated quarrels in the family circle. She could not bear her mother to show affection to her grandchildren and did not hesitate to strike the children.

Examination. She was an obese woman, mentally defective to a moderate degree, who did not cooperate in the examination. She had a right spastic infantile hemiplegia with corresponding atrophy and deformities of the right hand and foot. There were no abdominal reflexes on the right and the plantar response was extensor on that side. The left limbs were normal in all respects. There was anesthesia to discriminative stimuli (two-point), astereognosis and positional anesthesia on the right. There was no speech defect or dysphasia but the patient spoke in a low, grave, monotonous way. The head was rather small. The different organs and systems did not show abnormal signs. Special examinations confirmed the diagnosis of infantile hemiplegia. The plain roentgenogram showed atrophy of the left side of the skull. On the pneumoencephalogram a marked atrophy of the left cerebral hemisphere was demonstrated (Fig. 3). The electroencephalogram was described as having a reduction of electrical activity in the left frontal lead and slow activity of that hemisphere.

Hemispherectomy. She was operated upon on Nov. 10, 1955. The patient was intubated, and under general anesthesia a large left quadrangular frontoparieto-occipital flap was raised. The main arteries of the hemisphere were closed with metal clips and the veins were cancelled with cautery and oxycel. The whole hemisphere was resected in one piece after section of the corpus callosum, leaving intact the basal ganglia and insula. The choroid plexus was totally excised. The dural eversion, done to protect the sagittal sinus from further bleeding, prevented closing of the dura mater, which was left therefore amply open. The dural defect was covered with a sheet of Gel-film. The bone flap was held in place by two wire sutures.

FIGS. 3 and 4. *Case 2.* Pneumoencephalograms. (*Left*) Pre-operative. (*Right*) Postoperative. The dilatation of the "normal" ventricle is not as pronounced as in Case 1, but the shift is very marked.

The skin was closed in two layers without drainage. The procedure lasted 4 hours, and the patient tolerated it very well.

The operative findings were a marked atrophy of all cerebral convolutions of the left hemisphere and thickening of the arachnoid membrane. There was also a large hydrocephalus of the left lateral ventricle which gave the hemisphere the appearance of a bag. The electrocorticogram showed a spike focus in the left posterior temporal region. After hemispherectomy the electroencephalogram of the basal ganglia did not produce convulsive discharges.

Postoperative Course. After recovering from anesthesia the patient was conscious and the hemiplegia was more severe but less spastic. On the following day it was thought that the spasticity had diminished "in an extraordinary manner." However, she was aggressive once more, trying to strike the nurses and to take off the head bandage. She would not eat and became angry at the slightest provocation. The hemiplegia was more severe, two-point discrimination was defective on both

sides, and on the right there was superficial hyperalgesia and the astereognosis was more marked.

On the 5th postoperative day she was somewhat stuporous, docile, calm, febrile and had signs of meningeal irritation. Thirty cc. of bloody fluid were extracted from the operative cavity, and 10 cc. of cerebrospinal fluid, with the same appearance, were obtained by lumbar puncture. The cerebrospinal fluid showed no evidence of infection. The patient was febrile for 20 days with no adequate explanation and showed lack of appetite.

She was discharged home on the 25th postoperative day (Dec. 5, 1955). At that time she could walk with little support, was much more cooperative and her vocabulary seemed to be improved. The sensory changes remained as in previous examinations. The operative wound was clean and closed, with a small subgaleal collection of fluid.

At home she was febrile some days. Her appearance was very good. She had no complaints and no convulsions. On Jan. 2, 1956 she had three major seizures and her temperature rose to 103°F. She received 600 mg. Chlortetracyn and after 4 days the fever disappeared. She was calm and behaved well. The relatives were very pleased with her behaviour. She was referred to an orthopedic surgeon because of a marked inward flexing of the foot while walking, caused by hypotonia of the right leg. However, she could walk as well as before the operation and it was considered such a good result that moving pictures were taken for demonstration.

Brain-Stem Shift Syndrome. On Jan. 9, 1956 we were informed that she was negativistic, would not eat, would not leave the bed and when persuaded to swallow some food she vomited immediately. She was re-admitted on Jan. 11, 1956. She was apathetic, and extremely passive to orders, examinations and certain procedures, as, for example, the passing of a duodenal catheter through the nose (previously she had objected to these maneuvers violently). On neurological examination a right homonymous hemianopsia with a marked right hemiparesis was found. There were also sensory changes. She could not recognize a ring in the right hand, nor could she decide as to the position of the fingers, on angles up to 45 degrees, on both sides. Finer examinations could not be done because of the lack of understanding of the patient. She resisted the suggestion to walk. The most remarkable change in this moment was her extreme passivity and docility.

On Jan. 16, 1956 she was lying passively in bed, with eyes shut and apparently sleeping while not disturbed. She woke with some difficulty and carried out simple commands such as to open the mouth, and open and deviate the eyes to either side, but she could not do simple acts, as the nose-finger test. She put the finger at her nose and then looked at the examiner with an expression of perplexity, and left the finger in that position for 2 minutes. She was completely indifferent to the environment, without showing initiative to eat her meals or inform any one that she wished to pass urine or faeces. Thus she was doubly incontinent and had to be watched frequently to prevent soiling and maceration of the skin. There was a notable emotional blunting; she looked at the physician without any affective expression and obeyed some orders passively. The facies was expressionless and showed only some degree of peri-oral contraction when stimulated for a long time with a pin over the skin of the limbs. She did not show discomfort while she lay for a long time in passive decubitus and seemed not to notice when she was wet. She would let the attendants move her about without resistance. When asked how she was she said "well" and that she had no complaints. She was completely disoriented in all

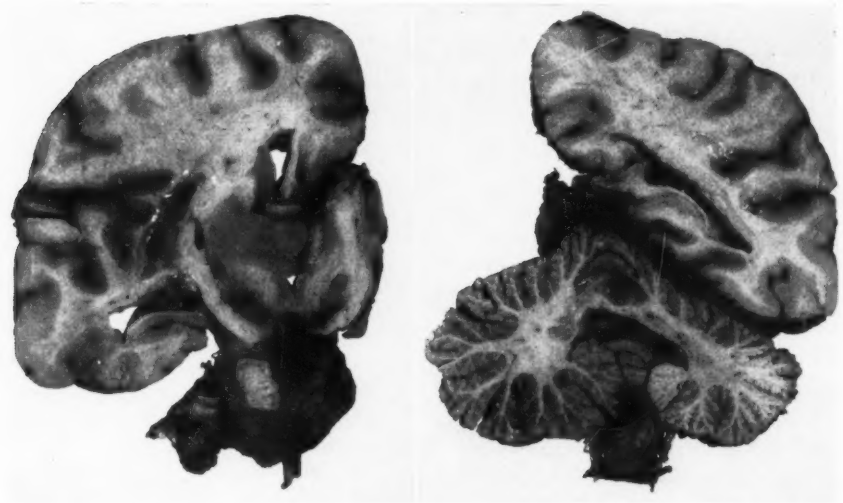
sectors and did not seem to recognize the examiner (whom she knew well). If asked if she knew him, she looked at him for a long time but kept silent. There was a marked retardation in the psychomotor responses. No disturbances were observed in articulation of words but it was not possible to do an adequate examination on dysarthria or dysphasia. Nevertheless, she understood simple questions and answered with one or two words at a time, after some 30 or 40 seconds. No psychotic changes in speech, perception or thought were evident. The mental deficiency seemed to be worse but could not be measured by the Wechsler-Bellevue scale or other psychometric tests. The patient had frequent hiccup and vomiting. There was no papilledema. The pupils were of different size, the right being slightly larger than the left, but both contracted briskly to light. There was also a left internal rectus paresis and a slow, rhythmic, gross nystagmus on deviation to the left. The right facial paresis, of a central type, corresponded to the right spastic hemiplegia which had evidently increased. There was moderately marked rigidity of the neck. The left limbs were also spastic, but in less degree than the right, and there was a frank bilateral extensor plantar response. She felt painful stimuli on both sides, though after considerable delay.

Now it was evident that the patient suffered a postoperative complication which affected mainly the upper brain stem. At the time it was thought that the syndrome was caused by displacement of the brain stem. On the following day (Jan. 17, 1956) right percutaneous arteriography of the carotid showed displacement of the right hemisphere to the left side, as judged by deviation of the right anterior cerebral artery 2 cm. to the left of the midline. The electroencephalogram, after intravenous injection of 0.2 gm. Sodium Seconal, revealed reduction of the electrical activity on the right, slow waves and complete absence of K rhythm.

A frontal trephining was done to exclude the possibility of a fluid collection over the right hemisphere or a right hydrocephalus, which might be causing the displacement. But the procedure demonstrated that the subdural space was empty and the right lateral ventricle was only moderately dilated, containing fluid at low pressure. On leaving the operating room she had two major seizures with rotation of the head to the left, clonic jerks of the right limbs, profuse perspiration, facial congestion and acceleration of the pulse rate.

On Jan. 19, 1956 pneumoencephalography was performed by lumbar route, which showed displacement of the right hemisphere to the left side (Fig. 4). The patient deteriorated steadily. She had a temperature of 104°F., frequent focal convulsions on the right side and became deeply unconscious. The rigidity of the neck was much more accentuated, and the head was permanently rotated to the left. Frequent decerebrate crises occurred, which lasted a few seconds, with both legs in rigid extension and the left arm in flexion. She died on Jan. 21, 1956 after several crises of opisthotonus.

Postmortem Examination. At autopsy, performed 2 hours after death, the left hemisphere was absent, the cavity being filled with a slightly xanthochromic fluid. There was no evidence of exudates or other signs of infection. The stump was covered by a slight, semitransparent film of fibrous tissue. Examination of this stump by serial sections demonstrated (Fig. 5) that it contained the corresponding thalamus, internal capsule and lenticular nucleus, which were approximately one-half the size of those of the normal side. There was also a very marked asymmetry of the cerebellar hemisphere, the right one (contralateral) being much smaller than the left (Fig. 6).



FIGS. 5 and 6. *Case 2.* (*Left*) The basal ganglia of the operative side were complete but reduced to about one-half the size of those of the normal side. (*Right*) Great asymmetry of the cerebellar hemispheres in relation to the primary disease, i.e., the infantile hemiplegia.

Several features of interest were evident:

a) There was a quite marked medial displacement of the right temporal uncus, which surpassed the free tentorial edge by 13 mm. This can be seen in Fig. 7.

b) There was a herniation of the gyrus cinguli under the free edge of the falx. Defective fixation left as only evidence of this a deep notch corresponding to the upper limit of the protruded portion.

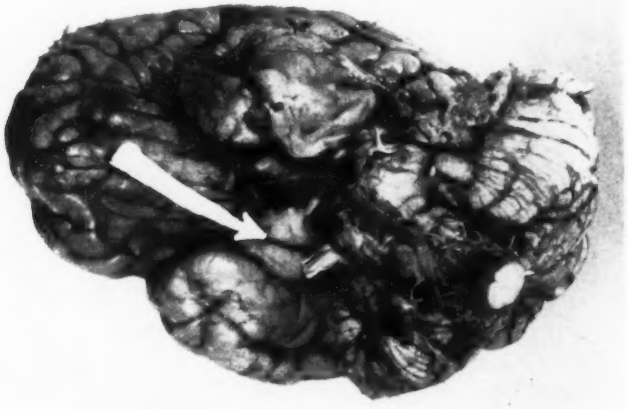


FIG. 7. *Case 2.* Marked herniation of the mesial aspect of the right temporal lobe. The arrow shows the notch made by the free tentorial edge.

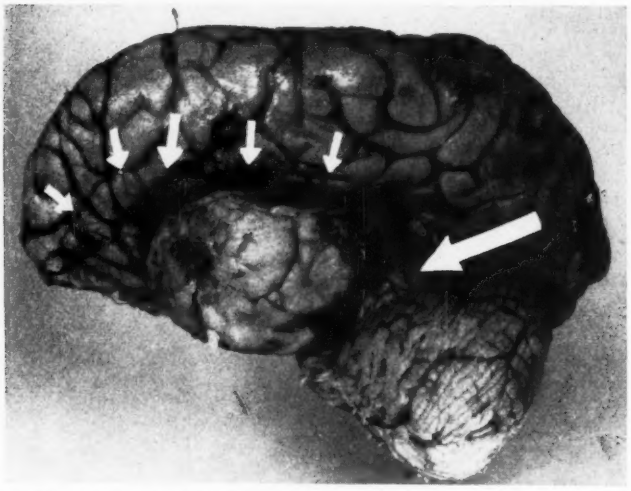


FIG. 8. *Case 2.* Herniation of the right upper portion of the cerebellum (large arrow) and herniation of the gyrus cinguli under the falx (small arrows).

FIG. 9. *Case 2.* Brain-stem shift towards the operative side.

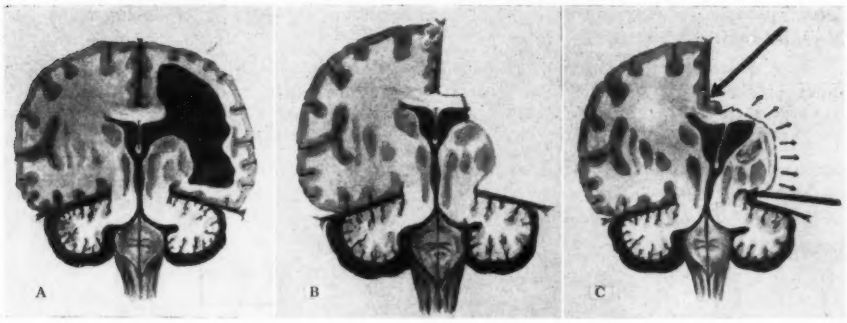


FIG. 10. *Case 2.* Diagrammatic representation of the sequence of events (A, B, C).

c) Herniation of the upper aspect (pars anterior lobuli quadrangularis) of the left cerebellar lobe through the incisura tentorii (Fig. 8).

d) Indentation of the right lateral aspect of the peduncle at the level of the free tentorial edge (Kernohan's notch).

e) There was a clear and definite shift of the medial structures towards the operative side, more pronounced in the cephalic end of the brain stem (Fig. 9).

f) There were no hemorrhages or areas of softening, and on serial section the macroscopic appearance of the nervous parenchyma was normal at all sites.

g) There was moderate dilatation of all the remaining ventricular system.

Fig. 10 shows a diagrammatic representation of the sequence of events.

Microscopic Examination. Sections were made of practically all the different parts of the central nervous system and they were studied by various histological

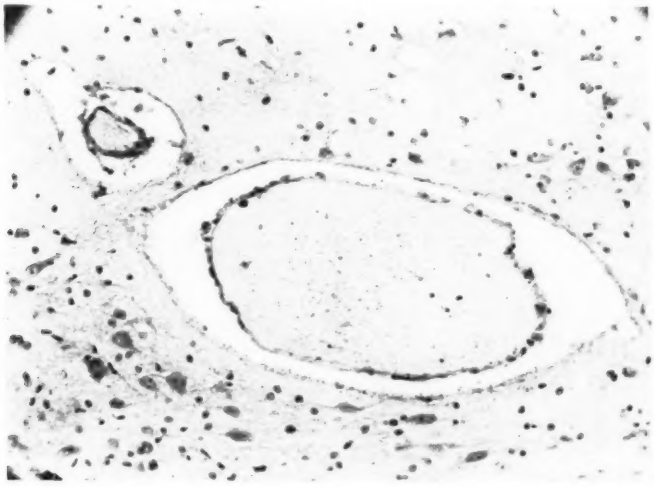


FIG. 11. *Case 2.* Largely dilated small veins with marked distention of the Virchow-Robin spaces, in the pons. (Cresyl-violet stain)

techniques with the collaboration of Dr. Leoncio Vega, Chief Pathologist at the Naval Medical Centre, Bellavista, Perú.

The changes which were obviously caused by the primary disease, i.e., the infantile hemiplegia, will not be described here for lack of space. The rest of the relevant findings can be summarized as follows:

a) There were many vascular changes, located mainly at the upper part of the pons and in the mid-line of the peduncular region. These changes were represented mainly by a very marked distention of the small veins (Fig. 11) and capillaries, as well as a tremendous enlargement of the perivascular spaces, which were filled with transudate and masses of gitter cells (Fig. 12).

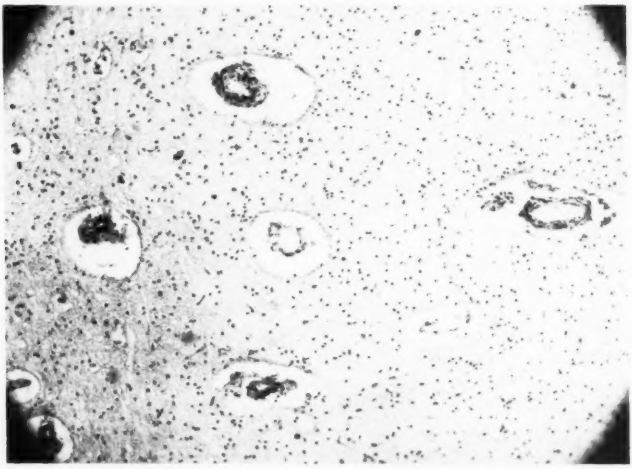


FIG. 12. *Case 2.* Vasoporosis in the midline of the cerebral peduncle. Tremendous distention of the Virchow-Robin spaces which show accumulations of gitter cells. Early glial reaction and vacuolation of the surrounding tissue. (Hematoxylin-eosin stain)

b) On careful search the presence of hemorrhages, or thrombosis, could not be demonstrated, although in the areas mentioned, definite evidence of recent tissue damage was found surrounding the vessels.

c) A few, scattered, small arteries of the peduncular and caudal thalamic regions showed degenerative alterations of the endothelium.

d) In the vicinity of the blood vessels of the mesencephalic and caudal diencephalic regions, there was globular swelling, rarefaction of tissue, and loss of the outline and degenerative changes of the myelin sheaths, which was much more striking and generalized at the level of both corticopontine tracts in the peduncle (Fig. 13).

e) There were only scattered changes in the ganglion cells, characterized by degeneration of the Nissl granules, caryolysis and loss of stainability, as well as pyknosis of the nuclei. These changes were more marked in the vicinity of the vessels in the reticular substance of the mesencephalic region (Fig. 14).

f) In the most caudal portion of the 3rd ventricle in the vicinity of the aqueduct, there was a very small area with perivascular infiltration of lymphocytes and degen-

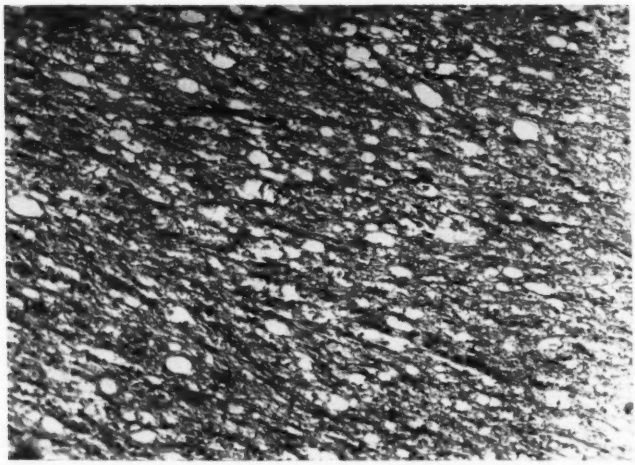


FIG. 13. *Case 2.* Globular swelling, loss of outline and degenerative changes of the white matter. Right corticopontine tract at the cerebral peduncle. (Hematoxylin-eosin stain)

erative changes in the ependyma (Fig. 15). In the subependymal region there were histiocytes laden with blood pigment.

g) There was also a similar small area at the stump of the corpus callosum.

h) Except for these latter zones, there was no evidence of inflammatory reaction. The most pronounced and generalized changes were those representing functional vascular disturbances in the brain stem.

FIG. 14. *Case 2.* Degenerative changes in the ganglion cells. Reticular substance of the mesencephalic region. (Cresyl-violet stain)

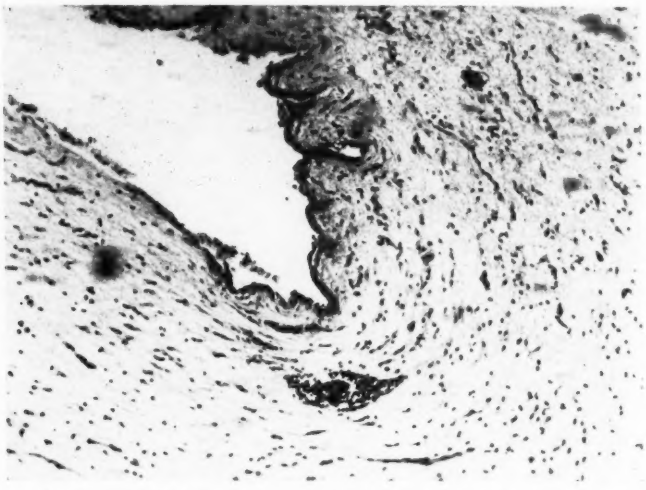


FIG. 15. *Case 2.* Small area with inflammatory changes in the subependymal region of the posterior portion of the 3rd ventricle. Some degenerative changes in the ependymal cells could be seen.

DISCUSSION

With the exception of a few reports that refer only casually to complications of hemispherectomy, we have not found in the literature any account of failures with a discussion of their mechanism. It is our impression that this lack of written information in this regard might not correspond to an actual representation of the incidence of failures. It is true that in most instances, especially those of patients with a markedly atrophied hemisphere, the procedure itself does not constitute an extremely serious technical challenge for a skillful surgeon, and the neurological dysfunction brought about by the operation is surprisingly well tolerated by the patient. But it is also a fact that the glow of glory around such heroic surgical procedures, as these may seem to be, serves often as an excuse to minimize the importance of failures or to avoid the publication of unhappy series.

Case 1 was indeed very difficult to interpret because of the circumstances that surrounded it. Even before operation there were dissenting opinions in our staff as to the proper indication of the procedure. The epileptic seizures, although present, did not constitute a major issue and the motor disturbances were fairly well tolerated. Were it not for the fact that the patient constituted a very serious behaviour problem we would probably have dismissed all thoughts of surgical interference. The operation itself was undoubtedly the most difficult of our series. It lasted short of 8 hours and was complicated by serious hemorrhage from the veins emptying the superior sagittal sinus. This could be controlled only by packing the bleeding region with oxydized cellulose in a manner that left us with the thought that thrombosis of the sinus itself might develop. This possibility was soon dis-

carded in view of the clinical course. On the other hand, the atrophy of the hemisphere was not as marked as in the other cases, and, consequently, we expected—and obtained—a much more pronounced neurological dysfunction during the immediate postoperative period.

Slowly, but progressively, the patient began to recover to the point that he could move his left side quite freely although he was not capable of walking. His mental condition, although still markedly impaired, showed a definite trend towards a better integration. It was then, approximately 50 days after operation, that serious, progressive symptoms and signs complicated the picture. He began to deteriorate, became immobile, mute, sleepy and indifferent, showing bilateral pyramidal signs. At this stage, it was difficult to visualize any cause for the new developments, and contrast roentgen-ray studies showed a marked shift of the medial structures. Our inexperience and the lack of information on the "normal" radiographic appearance of hemispherectomized patients left the case in an undecided status. The death of the patient and the lack of postmortem examination certainly did not help our ignorance.

Case 2 revived our sad experience. There had been no disagreement in the staff as to the indication of the procedure. The patient presented frequent seizures which were only partially controlled with heavy medication, the motor disturbance was poorly tolerated and the behaviour problem was of major importance. Air studies showed a very marked atrophy of the hemisphere and electroencephalographic appraisal was also favourable to surgery. The surgical act was simple. It lasted only 4 hours, the loss of blood was minimal and the hemisphere was resected in one piece, leaving behind a well irrigated stump formed by the basal ganglia. There was very little added neurological dysfunction in the immediate postoperative period, and the patient left the bed on the 10th day and the hospital 25 days after operation, being able to walk with little aid, with a very marked improvement in her behaviour, and free of seizures. Thus far, the results were quite gratifying. The dangers of late thrombosis, infection, hemorrhage, secondary degeneration of parenchymatous structures, etc., were so remote that we did not even consider them. It was on the 60th postoperative day that the complicating symptoms appeared, and these progressed and terminated fatally on the 72nd postoperative day.

When T.G. (Case 2) was re-admitted, it was clear in our own minds that we were dealing with a brain-stem dysfunction, similar to—if not identical with—that presented by Case 1. Having ruled out a subdural collection on the other side, having dismissed the possibility of an infectious complication, and having obtained evidence of the patency of the main arterial vessels and of the displacement seen in the contrast studies, the mechanism of production of the symptoms appeared to be explained by the shift of the medial structures, Fortunately, we were able to obtain permission for the autopsy, which confirmed our views by demonstrating the existence of a brain-stem shift, the marked medial displacement of the temporal uncus,

the protrusion of the gyrus cinguli under the falx, the apparent rotation of the brain-stem axis, and the notch made by the free edge of the tentorium on the right side of the peduncle and the cerebellum.

It may appear surprising that the naked-eye examination of the central nervous system, and specially of the brain stem, did not disclose any obvious pathological changes with the exception of the mechanical distortion described above. Furthermore, the microscopic study revealed the absence of severe changes of vascular origin (perivascular hemorrhages) which have been described repeatedly in fatal secondary brain-stem syndromes.[10,23,36,41] Recently, however, Wolman[48] has called attention to cases of severe brain-stem dysfunction which at autopsy did not show any macroscopic lesions of this region, but on histological examination disclosed changes of vascular origin. Scheinker[42] described as vasoporosis of the central nervous system, a histological picture very similar to the one found by us in Case 2.

Careful search was made of other lesions that could not be ascribed to a vascular origin, and the only changes found were two small areas where the perivascular cuffing of round cells could suggest an inflammatory reaction. The presence of histiocytes laden with blood pigment makes us think that this was only the result of reaction to the bloody cerebrospinal fluid of the postoperative period.

The explanation of every one of the complicating symptoms and signs presented by Case 2 as a result of a distortion of the brain-stem region should find its basis in our present knowledge of neurophysiology and clinical neurology.

Displacement and/or distortion of the brain stem at the level of the incisura tentorii has received a good deal of attention, especially in relation to intracranial mass lesions.

The symptomatology of the so-called pressure cone at this level was first described as such by Clovis Vincent[46,47] and his followers[15,16,30] as well as by Geoffrey Jefferson.[25] Its importance has been repeatedly emphasized in the neurological literature, especially by the works of van Gehuchten,[22] Cairns,[7] Schwartz and Rosner,[43] Cannon,[10] Munro and Sisson,[37] Evans,[18] and more recently by our own clinical studies.[5,6] The anatomical aspects of these displacements have received special attention from Meyer,[35] Carrillo *et al.*,[11,12] Tönnis *et al.*,[40,44] and Scheinker.[41]

However, several basic differences are obvious to any one familiar with the clinical and pathological picture of the transtentorial pressure cone. In the first place, it is evident that the mechanism of displacement in the cases presented here is completely different. We have not been able to prove that in either of these 2 cases there existed any "high pressure" component, and the weight of evidence makes us think that this factor did not play any role in the production of the shift. It is readily seen, on the other hand, that no simple explanation is to be found in the study of the dynamic anatomy of the falx and tentorium and their relation to the nervous structures. Any such simplified theory would have also to explain why the apparently large majority of hemispherectomized patients do not present this

complication and the brain "holds up" in normal position. Furthermore, Bates[3] has cut the falx in several of his hemispherectomized patients in order to stimulate the cortex of the remaining hemisphere, and he does not mention any complication similar to the subject of this report. Recent studies made in our Service on the anatomical measurements of the projecting dural folds and their relation to the brain stem, have shown that there is relatively small individual variation,[17] and our operating notes and photographs of both cases rule out the possibility of a gross anomaly of the dural folds. The autopsy of Case 2 showed an intact falx and a normal tentorium with standard measurements. McKissock[33] has described as a complication in his series (3 out of 29 cases), a noncommunicating hydrocephalus of the cavity left after operation. In all 3 cases, the choroid plexus had not been removed at the original operation, and this was apparently the cause of accumulation of fluid. We have excised the choroid plexus in all of our cases. One might speculate that negative pressure could develop in the empty hemicranium, but this theory would have to await more objective confirmation. The lateral ventricle in the "normal" side was punctured and it was found moderately dilated and at an estimated low pressure. The pressure was not actually measured. These findings, as well as the fact that all the ventricular system could easily be filled with air through the lumbar route, speak against hydrocephalic pressure from the normal side, but leave open the question of negative pressure in the operative side. It is certainly unfortunate that at the time we did not obtain more data pertaining to this point. Consequently, we must state that at the present stage of our knowledge we cannot find a trustworthy explanation for the ultimate cause of the shift. We have to content ourselves with the plain statement that this shift existed as proved by the roentgen-ray studies and the autopsy (Case 2). And it is our contention that this shift was the cause of the fatally progressing symptoms in both cases.

Another distinctive character of this syndrome seems to be the peculiar disturbances of consciousness. Except for the antemortem condition, there was not a real loss of consciousness, but a form of psychological stupor better described by the term "akinetic mutism," coined by Cairns.[7,9] Present advances in therapy have allowed us to see and study more and more cases of vascular and traumatic disturbances of the cephalic portion of the brain stem in patients who survive the initial diaschisis of this region which, until recently, was inevitably followed by death. Once the neurological dysfunction becomes circumscribed to the actual lesion, many of these patients remain for long periods in this apparently irreversible condition that is only ill-described by any term related to "consciousness." This mental and emotional inertia, this inability to respond adaptively to any stimulus,[21] is usually arrived at after a more or less prolonged state of complete coma. If our interpretation is correct, our 2 patients, because of the peculiar origin of the brain-stem dysfunction, showed the same mental disturbances but progressing in a reverse sequence. At the beginning, especially in Case 2, the mental picture was unrecognizable as such and it impressed us more like

a mainly psychological reaction. Slowly but progressively, however, she became more mentally inert and soon we were facing a fully developed akinetic mutism, clinically identical to the mental disturbance that every neurosurgeon has had the occasional misfortune to see following severe trauma of the brain stem that was compatible with survival.

Perhaps the syndrome witnessed by us finds more similarity with that described by Netzky and Strobos[38] in relation to tumors of the midbrain.

We are of course tempted to speculation when we study cases like those described here. The large amount of recent information and the growing interest in the physiology of the reticular substance of the brain stem are rapidly modifying previously held theories. Furthermore, the interpretation of new or unusual clinical observations should always wait for testimonies from other sources, and accumulation of more data. Even if the present interpretation of our findings may later be modified, we hope that the publication of these cases may arouse some interest in the late complications of hemispherectomy.

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CASE REPORTS

"CENTRAL PAIN" FROM CEREBRAL ARTERIOVENOUS ANEURYSM*

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With the widespread use of cerebral angiography, the diagnosis of cerebral arteriovenous aneurysm is now more common than at any previous time. With increased appreciation of its clinical manifestations, the diagnosis of this formidable cerebral lesion must be considered in any case of a patient with Jacksonian seizures, associated with hemiparesis or hemihypesthesia, in which there has been an episode of subarachnoid bleeding.

The indications for surgical therapy in these lesions have been reported by a number of authors, notably Olivecrona and Riives[3] and Norlén.[2] The possibility of pain in a paretic extremity in association with this lesion has not been reported previously. During his visit to this country, Professor Olivecrona very kindly reviewed the case described in this paper and recommended that it be reported because of its unusual nature.

CASE HISTORY

Mrs. M.L., aged 50, was first seen in neurosurgical consultation at the Fuller Memorial Sanatorium, referred by Dr. L. A. Senseman. She had entered the sanatorium for consideration of intensive psychotherapy, because of unbearable pain in her right upper extremity. At the time that neurosurgical consultation was requested, the possibility was raised of performing prefrontal lobotomy as a method of controlling pain, since her pain had not responded to large doses of analgesic medication nor to various forms of psychotherapy.

The pertinent history appeared to have begun about 10 years previously. At that time, at the age of 40, the patient, who apparently had been in good health, began to suffer from transient "fainting spells." During one of these episodes the period of loss of consciousness was unusually prolonged (2 hours) and when she recovered she was noted to have a complete right hemiplegia and a total aphasia. She was hospitalized and seen in neurological consultation. According to the husband, he was told that the "blood clot was too near the brain and they could not operate." She remained in the hospital for 3 weeks and then slowly recovered and was able to leave the hospital ambulatory. She dragged her right leg, but during her convalescence at home the strength in the right leg improved and she was able to walk with a limp. She had a complete paralysis of the right upper extremity and, in the succeeding months, regained only some motion at the right shoulder. A typical hemiplegic attitude of the right upper extremity developed, with flexion contracture at the elbow, wrist and finger joints. She made slight improvement in her aphasia, and was able to speak in short phrases, but was intelligible only to her husband. She could count up to four, but no further.

With all of these severe handicaps, she made a fair adjustment during the succeeding years, and lived a very sheltered life, keeping house for her husband and seeing only relatives and close friends. Two years prior to admission to the hospital, she began to complain of pain in the paretic right upper extremity. She was seen in medical consultation at this time, and

* Presented at the meeting of the Harvey Cushing Society, Honolulu, Hawaii, April 16, 1956.

it was considered that the pain was related to the developing contracture of the joints of her right upper extremity, particularly the joints of the fingers and wrist. A period of physiotherapy was undertaken, with no specific relief in symptoms. The pain occurred in paroxysms and was described to her husband as being "burning" in quality and completely unbearable. She was seen by numerous physicians for this complaint of pain, and all of the customary analgesic medications were tried without success. Finally, commitment to a mental institution was considered and psychotherapy was carried out as well as possible in the face of the existing aphasia and difficulty in comprehension. At this time, neurosurgical consultation was requested.

Course. Review of the history aroused some suspicion of a vascular malformation, by virtue of the clear-cut story of a cerebrovascular accident in a young person previously subject to fainting spells. Cerebral angiography was advised and carried out percutaneously under local anesthesia. Radiographs made on June 9, 1951 showed a well demarcated arteriovenous aneurysm of the left parietal region (Fig. 1).

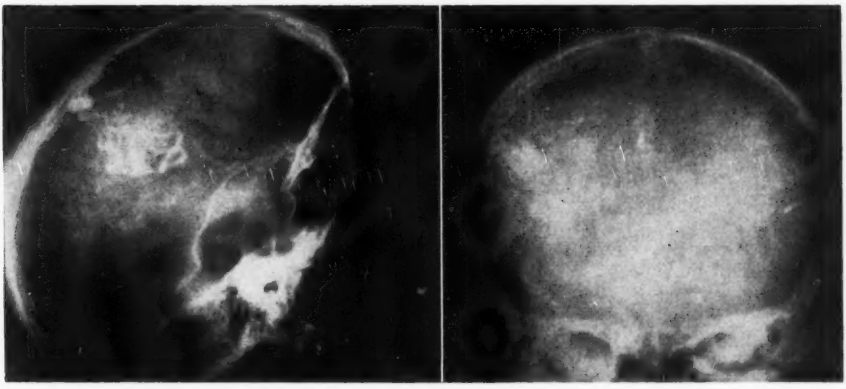

FIG. 1. Lateral and anteroposterior angiographic films in the late phase, showing circumscribed arteriovenous aneurysm of left parietal cortex.

Comment. The question of surgical intervention was debated at great length. It was considered that the possibility of a second rupture of the arteriovenous malformation was relatively remote, in view of the long time-interval since the previous rupture. On the other hand, the steady intensification of her pain was postulated to be in some way related to the cerebral lesion, and the question was considered whether slow expansion of the vascular malformation might not be producing pressure upon the sensory cortex so that her subjective sensation of pain might be in fact a severe painful paresthesia. Upon this basis, surgery was proposed, although excision of the lesion was felt to offer little hope for recovery of motor power or function of speech.

Certainly, it was felt inadvisable to perform any type of psychosurgical procedure in view of the tremendous enlargement of the vascular channels of the left hemisphere. It was finally agreed to perform a cranial exploration.

Operation. This was carried out in two stages. In the first stage, a large bone flap was elevated under general anesthesia, and the dura mater was reflected to confirm the adequacy of exposure of the vascular lesion. The dura mater was then closed with interrupted sutures of silk and the bone flap was returned to position.

The second stage was carried out 1 week later under local anesthesia. At this time it was proposed to excise the lesion with careful attention to the function of the speech mechanism before performing ligation or extirpation of any portion of the lesion. With the previous angiogram available, it was possible to determine the main feeding trunks of the angioma, and

attempts were made to ligate the arterial supply with interrupted sutures of black silk. It was during the ligation and occasional traction upon these vessels that it was noted that the patient complained bitterly of pain in the right upper extremity. The pain was described as being identical in character with the spontaneous burning pain that had brought her to neurosurgical attention.

Electrical stimulation was carried out, using a sine-wave stimulator at 60 c./sec. and a voltage of 1–3 V. No subjective responses were elicited under electrical stimulation, although at the periphery of the lesion, motor responses could be produced, particularly in the shoulder and musculature of the upper arm. However, when the forceps were used to compress one of the large arteriovenous trunks, and particularly if a silver clip was applied to the vessel and then moved with a clip holder, a spontaneous exclamation of pain was elicited. This observation was repeated numerous times and all of the observers in the operating room were satisfied that the patient could detect any manipulation of the vessels comprising the aneurysm.

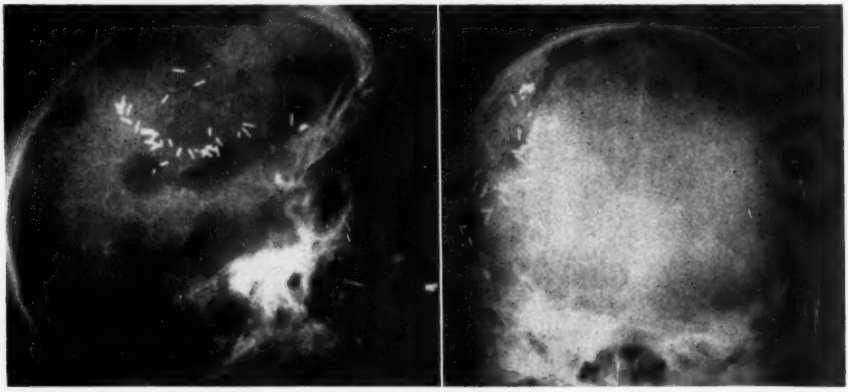

FIG. 2. Lateral and anteroposterior angiographic films made postoperatively. The absence of filling confirms the total excision of the arteriovenous aneurysm. The position of the bone flap and surgical clips are shown.

A systematic attempt was then made to reduce and finally exclude the circulation to the arteriovenous malformation. This was carried out, beginning in the inferior, or temporal portion of the aneurysm, and continuing parietalward toward the sagittal sinus. When a sufficient reduction in the feeding channels was effected, and when a dull spatula could be inserted between the aneurysmal vessels and the apparently normal brain, a large purse-string silk suture was put down over the lesion and gently inserted into the depth of the cortex. When the largest portion of the lesion had been shelled from the adjacent cortex, the purse-string suture was slowly tightened and further blunt dissection was performed. Silver clips were applied wherever necessary, and only rarely was coagulation required to seal some of the thin-walled vessels, which from time to time would rupture from increased venous pressure and bleed furiously. By patient dissection it was possible to remove the entire lesion *en bloc*.

Histological diagnosis: cavernous angioma.

Course. The patient made an uneventful recovery, and it was noted even in the first 2 days postoperatively that there was a definite improvement in her speech. She was capable of verbalizing longer phrases, and on the day following surgery was able to count to ten, omitting only the digit seven, which she did not appear to have the capacity to express until some 3 months postoperatively. There was almost immediate relief of pain in the right upper extremity. Even the gait improved, and there was increased power in the right lower extremity on direct testing. Eighteen months later, the improvement was sustained and the

patient was hospitalized for corrective orthopedic surgery to improve the position of the fingers of the right hand, as she was sensitive about her appearance in public. Postoperative angiography was carried out at this time, and confirmed the completeness of the surgical extirpation of the arteriovenous aneurysm (Fig. 2).

It is now 5 years since the operative removal of the vascular malformation. She has remained free of pain, and has made steady improvement in her speech, motor power and gait.

DISCUSSION

This case presents a relatively rare symptom associated with arteriovenous aneurysm of the brain, namely, pain referred to the contralateral extremity, presumably arising within the involved hemisphere. The mechanism involved in this symptom is not clear.

It has been proposed by some[1] that this may be a form of thalamic pain associated with the vascular abnormality involving the deeper structures of the hemisphere. Against this conception is the fact that the arteriovenous malformation is generally confined to the superficial zones of the cortex, and that the symptoms disappeared by resection of the malformation, without presumably affecting the circulation through the thalamus.

I am more impressed with the obvious mechanical, as well as the chemical, alterations that must occur in the cerebral cortex in association with this type of vascular malformation. The reproduction of the painful state by traction upon the exposed vessels in a conscious patient would appear to support this possibility. The fact that referred pain to an extremity can occur from mechanical stimulation, in association with presumed altered circulation through the sensorimotor cortex, suggests that this stimulus may be an unusual form of massive proprioceptive stimulation. Certainly, it requires explanation in light of currently held theories regarding localization of pain centers within the brain.

No definite conclusions appear to be warranted from this report, but it is published in the hope that it will stimulate further investigation and permit more reliable conclusions as subsequent data are accumulated.

From the technical standpoint, it is felt worthy of reporting that the two-stage procedure for dealing with these treacherous cerebral lesions appears to offer greater safety to the patient, and greater comfort to the operator. The ability to feel secure regarding the maintenance of normal function while operating in such vital areas as the left frontoparietal cortex, needs little comment. The actual excision, when possible, of the vascular malformation is more readily accomplished when unattended by the complications of general anesthesia, regardless of type. The preliminary turning down of the bone flap and exposure of the lesion under general anesthesia carries little risk and avoids the fatigue of both patient and operator, which would certainly occur if the *entire* procedure were attempted under local anesthesia.

With present advances in neurosurgical technique, the indications for a two-stage craniotomy have steadily declined, but in this author's opinion, the arteriovenous aneurysm of the brain remains a situation in which two-stage craniotomy is advisable.

CONCLUSIONS

A case is presented of intractable pain of an extremity, apparently arising from, or in association with, a cerebral arteriovenous aneurysm.

The possible mechanism for this condition is discussed.

An incidental plea is made for performing the resection or coagulation of these lesions in two stages, the bone flap and dural exposure being carried out under general anesthesia, with the actual surgical attack upon the lesion being carried out under local anesthesia.

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MYELOPATHY CAUSED BY ATLANTO-AXIAL DISLOCATION

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Injury to the upper cervical spine resulting in a separate odontoid process and atlanto-axial dislocation presents a serious problem. The patient may survive the initial episode and the injury may remain undetected and untreated. A sudden recurrence of the deformity may produce signs of damage to the spinal cord, or, over a period of many months or years, evidence of cord damage may slowly develop as the result of recurrent gliding of the atlas on the axis, with consequent narrowing of the vertebral canal.

Corner,[6] in 1907, describing a series of patients with dislocation of the atlas, recorded the case of a young woman in whom signs of damage to the upper cervical cord developed 1 year after fracturing the odontoid process, with death occurring 14 months following the injury. This author stressed the possibility of delayed myelopathy resulting from abnormality produced by trauma at the atlanto-axial level.

Recognizing the significance of dislocation of the atlas on the axis associated with odontoid fracture, Mixter and Osgood[12] in 1910 successfully treated 1 patient by operation in which, by means of a stout braided silk suture, the posterior arch of the atlas was firmly fixed to the spine of the axis.

In 1912, Elliott and Sachs[8] reported the case of a man, aged 50, who had had a fracture of the odontoid process some 32 years before his final hospital admission, in the authors' words "a long earthly existence with a broken neck." Autopsy revealed a pseudo-arthrosis between the body of the axis and the odontoid, the latter being ankylosed with the arch of the atlas. Sections of the spinal cord showed that the crossed pyramidal tracts were completely degenerated and atrophic. Similar spinal cord degeneration was found by List[9] in 1941, the result of cord compression by abnormalities, such as a loose odontoid, in the region of the foramen magnum and upper cervical spine.

Bachs *et al.*,[1] in 1955, reported finding in the literature only 9 cases of delayed myelopathy following atlanto-axial dislocation associated with a displaced odontoid process. These authors added 1 more case to the series but, unfortunately, autopsy was not permitted. However, in recording 2 cases from the literature in which autopsy was performed, mention was made of demyelination, disintegration and glial reaction within the spinal cord and thickening of the pia mater and arachnoid.

The present case likewise demonstrates the extent to which the cord may be damaged by atlanto-axial dislocation, the result of an injury some 25 years before the onset of symptoms.†

CASE REPORT

R.G. (50-6533), a man aged 41, was admitted to the Montreal Neurological Institute on April 26, 1950, referred by Dr. Reuben Rabinovitch. He complained of loss of strength in

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† This case was presented at the meeting of the Halsted Society in Montreal on February 24, 1955.

the right arm and leg, and soreness of the neck. Family and personal history were negative apart from gonorrhoea and syphilis 20 years previously. The man was married, had 7 children, and had been a chauffeur for the past 12 years. At the age of 14, over 25 years before the present admission, while balancing himself upside down on a fence, he fell and landed on his head, knocking himself unconscious for 15 minutes. Following this incident, and until 14 months before this admission, he was quite well except for some limitation in extreme rotation of his neck. Symptoms began with weakness and stiffness in the right lower limb which were followed in a few months by weakness of the right arm. About 4 months before admission the left arm became weak and he observed that the right hand was less sensitive in touching various objects. He was aware of an increasing unsteadiness of gait, which was more marked in the dark. For a period of 1 year he had experienced a sensation of pain and tiredness in the neck and a soreness in the lower back.

Examination. He was a well-developed male who walked in a very stiff-legged fashion on a wide base. There was marked tenderness on palpation of the upper cervical spine and a prominence of the spine of C3. The right pupil was smaller than the left and there was a slight unsustained nystagmus on extreme gaze to the right. There was slight weakness of the right sternomastoid and trapezius. Motor power was decreased throughout, but more markedly so on the right side, particularly in the right hand. There was slight wasting of both hands and forearms, more so on the right. Fine and rapidly alternating movements were done more slowly on the right than on the left. Sensation of touch was intact but there was altered temperature sensation with indistinct limits over the trunk anteriorly and posteriorly. Pain sensation was difficult to evaluate. There was thought to be an area of hyperaesthesia in the C3 distribution. Vibration sense was markedly decreased or almost absent below C3, particularly on the right side. Position sense was surprisingly well maintained, with only slight loss in the toes and more moderate loss in the fingers. The deep tendon reflexes were bilaterally hyperactive, the right slightly more than the left. There was plantar extension bilaterally, with ankle clonus and right wrist clonus. Tone was markedly increased throughout.

Roentgenograms of the cervical spine disclosed a marked atlanto-axial dislocation (Fig. 1A) which could be completely reduced by full extension of the head (Fig. 1B). With the head flexed there was anterior displacement of the atlas on the axis and an obvious narrowing of the cervical canal between the posterior arch of the atlas and the body of the axis. Tomographic films demonstrated a normally shaped dens, separated from the body of the axis by a distance of 3 to 5 mm.

Operation. Atlanto-axial fusion was done under general anaesthesia on April 29, 1950. (In this particular case traction was not applied but subsequent procedures of this type have been done under traction.) The posterior arch of the atlas was wired to the base of the spinous process of the axis and the cartilaginous plates of the articular facets between C1 and C2 were removed. There resulted a better alignment of the posterior arches of the atlas and axis. The intervening dura mater, which before had been stretched tightly, was relaxed and pulsated well. However, at the close of the operation, the anaesthetist reported that the patient's respirations were impaired. When the patient regained consciousness, it was apparent that he was unable to move any of the extremities. Respiration was assisted with the respirator for 48 hours but his condition deteriorated and he died on May 1, 1950.

Autopsy. The specimen of the upper cervical spine obtained at autopsy was cut in the midline, as shown in Fig. 2A. The mechanism by which the upper cervical cord was compressed is readily seen. The loose odontoid, with the pseudo-arthrosis between the dens and the body of the axis, is apparent in Fig. 2B. It is to be noted that, with any degree of movement, not only bone but the associated soft tissues encroach upon the cervical canal and thereby compress the cord. The marked degree of flattening of the cord with loss of substance is seen in Fig. 3A and B. At the level of the lesion the pia-arachnoid is greatly thickened. Above the level of cord compression, at the pyramidal decussation, degeneration can be seen in the lateral spinothalamic tracts and in the posterior columns, bilaterally (Fig. 3C). A cross-section through the lower cervical cord (Fig. 3D) shows marked demyelination in the crossed

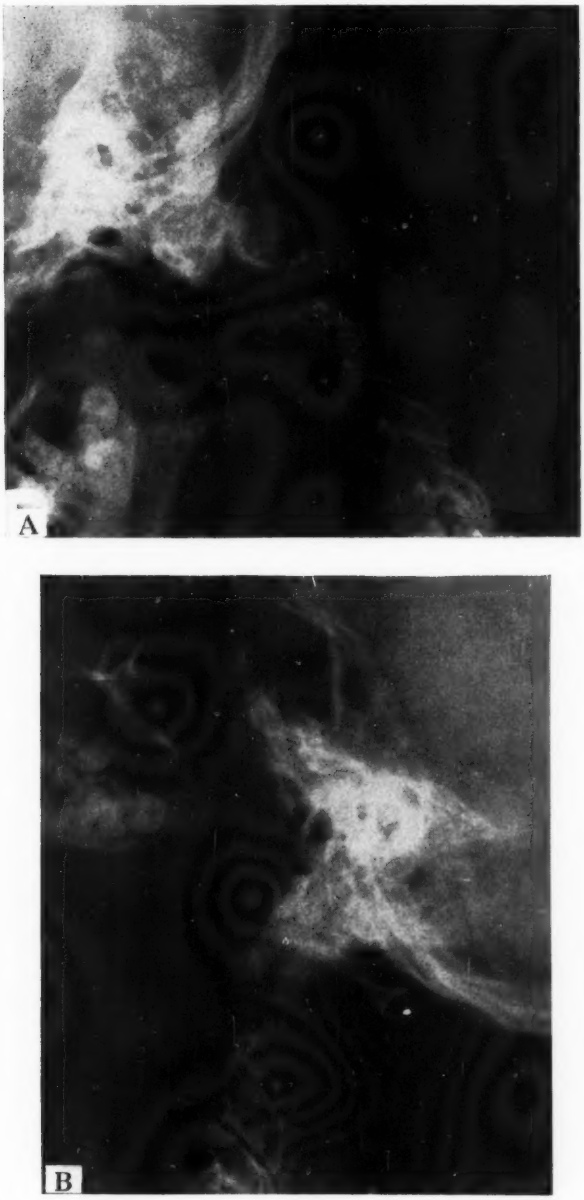

FIG. 1. Lateral view of cervical spine, (A) in flexion, showing gliding of the atlas on the axis, and (B) in extension.

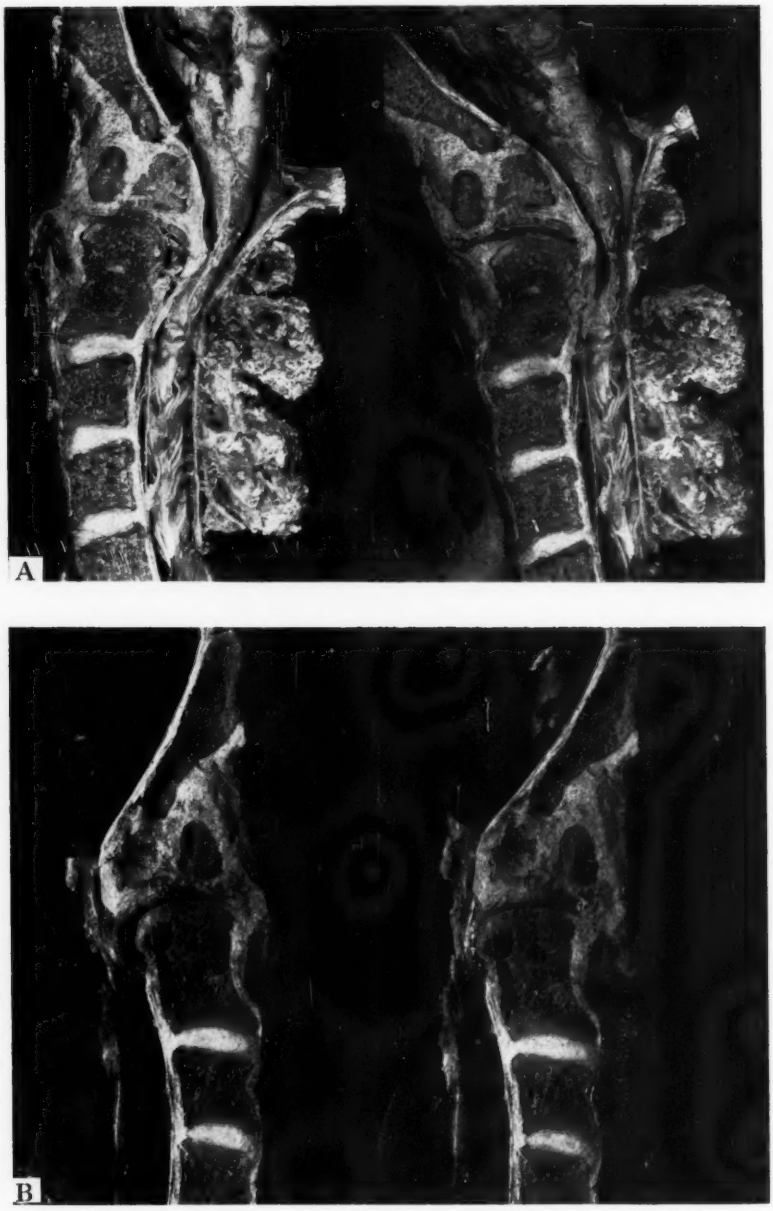

FIG. 2. Autopsy specimen of upper cervical spine showing (A) compression of cord, and (B) pseudo-arthrosis between the dens and the body of the axis.

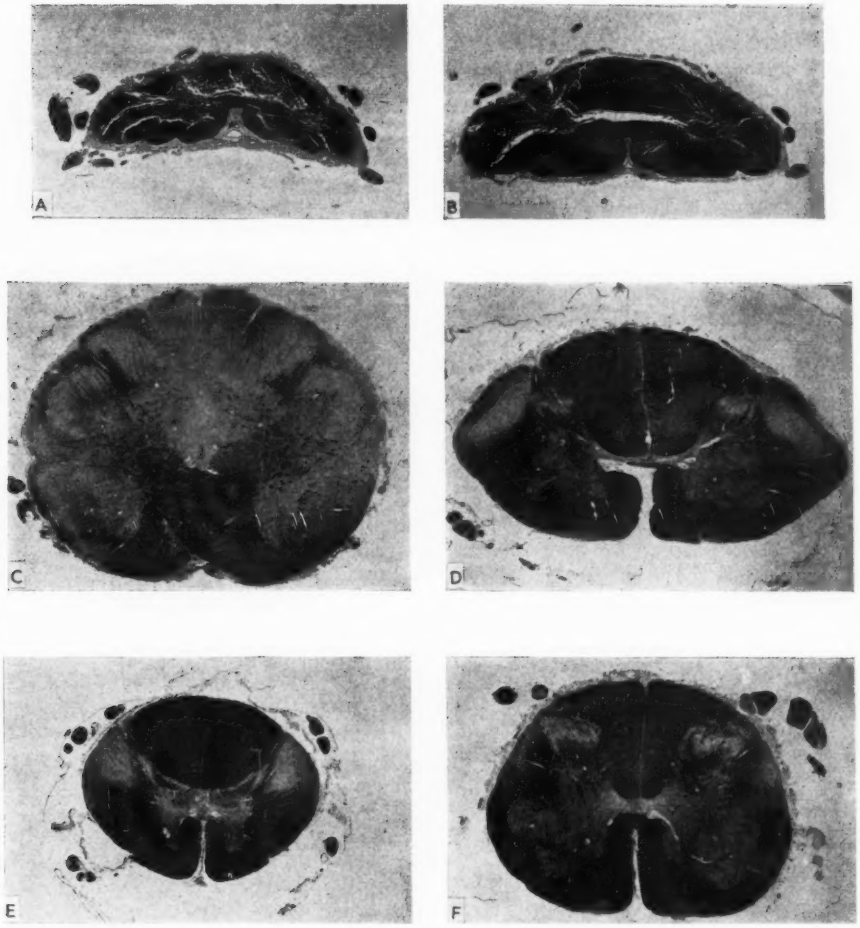

FIG. 3. (A, B) Cervical cord at level of cord compression. Weil, ×5. (C) Above level of cord compression, at pyramidal decussation; degeneration in lateral spinothalamic tracts and posterior columns bilaterally. Luxol & cresyl violet, ×5. (D) Below level of cord compression; degeneration in crossed pyramidal tracts. Luxol & cresyl violet, ×5. (E) Thoracic cord; degeneration in crossed pyramidal tracts. Luxol & cresyl violet, ×5. (F) Lumbar cord; degeneration in crossed pyramidal tracts. Luxol & cresyl violet, ×5.

pyramidal tracts. A similar picture is to be noted in the thoracic cord section (Fig. 3E) and in the lumbar cord section (Fig. 3F).

An incidental finding, at the level of cord compression in Fig. 3A and B, are the several skeins of nerve fibers within what remains of the grey matter. The interlacing network of fibers is shown in greater magnification in the Bodian stained sections in Fig. 4A, B, and E. Adjacent to the skein in Fig. 4C can be seen a group of nerve fibers. A similar bundle of nerve fibers rims the periphery of a blood vessel lying within the anterior median fissure in

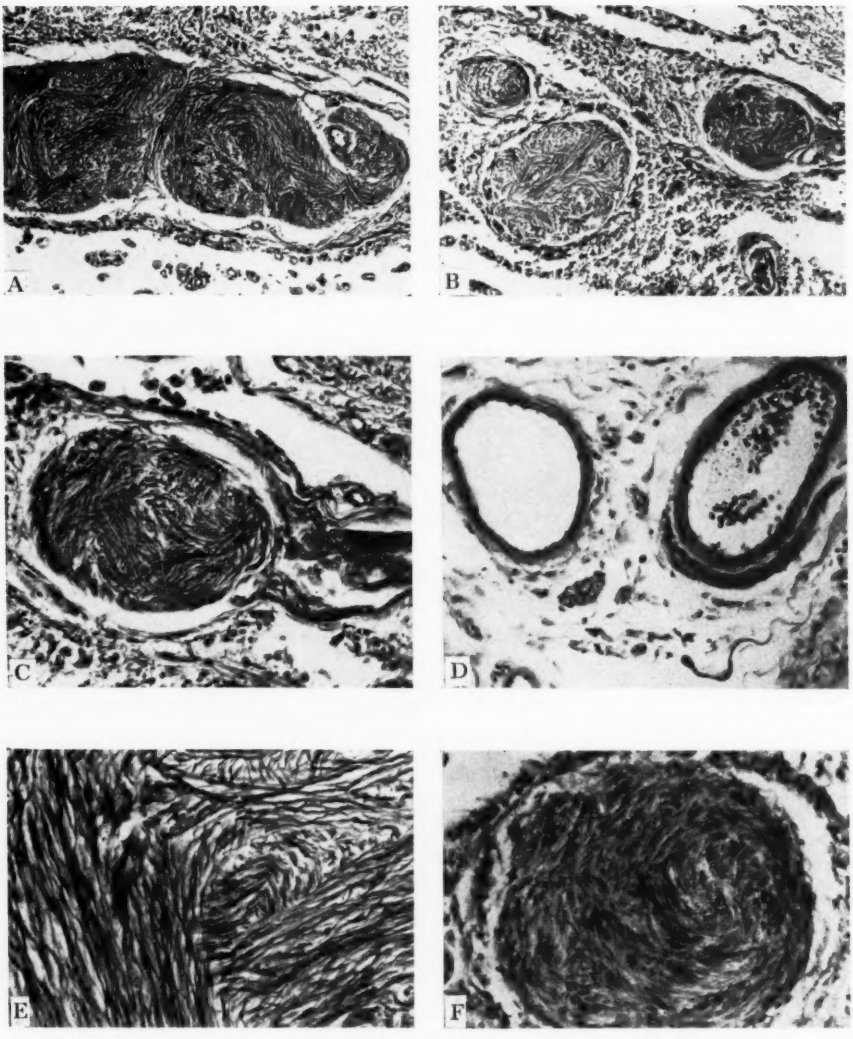

FIG. 4. (A) Skein of nerve fibers, at level of cord compression. Bodian, ×86. (B) Smaller skeins of nerve fibers. Bodian, ×86. (C) Group of nerve fibers adjacent to skein. Bodian, ×172. (D) Bundle of nerve fibers rimming blood vessel. Bodian, ×172. (E) Interlacing network of nerve fibers within a skein. Bodian, ×303. (F) Schwann-like cells associated with nerve fiber skein. Cresyl violet, ×172.

Fig. 4D. Cresyl violet staining of a skein (Fig. 4F) discloses that these fibers are associated with cells closely resembling Schwann cells.

DISCUSSION

This patient had a symptom-free interval of approximately 25 years between the accident and the onset of his neurological complaints. It is difficult to know whether the cervical cord lesion with degeneration of ascending and descending tracts resulted from mechanical factors, per se, or whether it followed upon interference with blood supply to this level, thereby producing the degeneration.

Studies of cervical cord compression in cervical spondylosis have shown a similar degeneration of ascending and descending tracts (Bedford, *et al.*;[2] Brain, *et al.*[3]). These authors believed that the cord damage resulted from direct pressure, the cord being fixed by the dentate ligaments. Mair and Druckman,[11] on the other hand, concluded that the important factor is compression of the anterior spinal artery, resulting in an impaired blood supply in its distal distribution, i.e., those areas of the cord showing degeneration.

While reviewing sections of the cord in cases of protruded cervical intervertebral discs, Mair and Druckman[11] found evidence of aberrant nerve fibers at the levels of cord compression. These fibers appeared in bundles or large skeins and frequently were covered by Schwann cells.[7] They are identical with those found in the present case, in which cord compression resulted from atlanto-axial dislocation associated with a loose odontoid process. It is thought that these collections of aberrant fibers represent an attempt at regeneration within the injured spinal cord.

The extensive destruction within the cord in this case emphasizes the importance of recognizing odontoid injuries and treating them to prevent the later development of this severe and progressive myelopathy. Congenital abnormality of the upper cervical spine with a separate odontoid process may produce a similar degree of myelopathy. In fact, McRae[10] has stated that it is not possible to decide in an adult whether the radiological picture is that of an old ununited fracture of the odontoid or an anomaly.

Treatment consists of skeletal traction and fusion, as advocated by Cone and Turner.[5] During operation it is probably important to maintain skeletal traction to facilitate the placement of bone wedges between the facets of C1 and C2, thereby keeping taut the redundant soft tissues which otherwise tend to encroach upon the cervical canal.[4] When wound healing is complete, the tong-traction may be removed and the patient may be immobilized in a Minerva plaster.

SUMMARY

Reported is the case of a man in whom motor weakness in the extremities and impaired sensation over the body developed approximately 25 years after a fall on his head which, presumably, fractured the odontoid process. It is believed that the loose odontoid permitted excessive movement at the atlanto-axial joint, resulting in compression of the upper cervical cord and degeneration of both ascending and descending tracts. An incidental finding was the presence of so-called "aberrant regenerating nerve fibers" at the level of cord compression.

I wish to thank Dr. William Cone for permission to report this case and for his interest and help in preparing this paper.

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A CALCIFIED THORACIC INTERVERTEBRAL DISK WITH HERNIATION AND SPINAL CORD COMPRESSION IN A CHILD

CASE REPORT

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(Received for publication June 14, 1956)

Herniated thoracic intervertebral disks causing compression of the spinal cord are uncommon, comprising about 0.25 per cent of all disk protrusions. Most cases occur in the middle-age group, and the youngest patient found in reviewing reports in the literature was a 26-year-old male.[4] A high percentage of herniated thoracic disks show calcification of the affected nucleus pulposus, and the presence of calcification in this location appears to increase the liability of the disk to rupture.[3] The etiology of such deposits is not clearly understood, but their clinical significance differs from that of the common calcification of the annulus fibrosis seen in chronic lumbar diskogenic disease.

Calcification of the nucleus pulposus may be observed in children also, in whom it is associated frequently with clinical symptoms, such as local pain and tenderness. Twenty of these cases are recorded in the available literature, but in none of these has mention been made of compression of the spinal cord or of surgical treatment.[6–9]

The case of a 12-year-old boy with a calcified nucleus pulposus at T6 which had ruptured into the spinal canal, causing signs of cord compression, is, therefore, interesting because of its uniqueness. The lesion in this case was successfully excised with relief of symptoms and the objective neurologic deficit.

CASE REPORT

P.I. (NYH #726585), a 12-year-old white male, was admitted to the New York Hospital on Dec. 14, 1955, complaining of pain in the back in the mid-scapular region, which was aggravated by flexion of the neck. Seven days previously he had fallen on his right thigh, but sustained no appreciable injury. The next day he complained of aching pain in the xiphoid region, which was unrelieved by local heat or aspirin. Twenty-four hours later this symptom was replaced by nonradiating interscapular pain. Three days before admission the pain became worse, and he found that flexion of the neck greatly accentuated it. His only comfortable position was prone, with the neck extended. The pain was not increased on coughing. Walking was uncomfortable, and his gait was described as stiff and erect. No impairment of bladder function was noted. There was no history of past injuries, excessive intake of milk or Vitamin D, or previous back pain. Roentgenograms of the spine 5 days after the fall revealed calcification of the T6 nucleus pulposus with extrusion of the calcific material into the spinal canal.

Examination. The patient was a healthy appearing boy, who walked erectly with his neck moderately extended. Flexion of the neck caused pain in the interscapular area, but other motions of the neck were free and without accompanying discomfort. Coughing and jugular compression did not produce pain, and there was no tenderness over the spine. There were no motor deficits, but the deep tendon reflexes in the lower limbs were more active than those in the upper. The abdominal reflexes were present and the plantar responses were flexor.

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An incomplete sensory defect to pin and cotton existed below the costal margins bilaterally. There was no elevation of temperature.

Additional roentgenograms of the spine with anteroposterior and lateral tomograms showed a normal thoracic spine except for a circular area of calcific density in the center of the T6 intervertebral disk (Fig. 1). On the lateral projections posterior extension of the calcific material into the spinal canal was evident (Fig. 2). A skeletal survey revealed no other soft-tissue calcifications. Examination of the urine for homogentisic acid was negative.

Lumbar puncture revealed clear, colorless spinal fluid with no evidence of spinal block on

FIG. 1 (*left*). Anteroposterior view of thoracic spine showing dense calcification of T6 disk. Fig. 2 (*right*). Lateral tomogram, showing extension of calcific material into spinal canal.

manometric studies. A myelogram with 6 cc. of Pantopaque was performed. This showed anterior compression of the radio-opaque column on the lateral view and splitting of the dye in the midline as it passed the level of the calcific mass (Fig. 3). The Pantopaque was recovered, and the spinal fluid protein was reported as 27 mg. per cent.

Operation. On Dec. 19, 1955, a wide laminectomy of T6 and T7 was performed. When the dura mater was opened the cord was seen to be humped over a soft bulging extradural mass at the level of the T6 disk. After two dentate ligaments had been divided on each side, an extradural exploration was carried out. The soft mass lay outside the annulus and consisted of amorphous calcific material similar to that seen in peritendinitis calcarea of the supraspinatus tendon. About 1 cc. of this material was removed with small curettes and strong suction. The annulus had ruptured near the midline and readily admitted a staphylorrhaphy. Exploration of the intervertebral space through this opening yielded more of the toothpaste-like substance. A thorough evacuation of the interspace was not attempted because of the

narrow confines in the thoracic region of this child, and because it was felt that the remaining calcium would soon disappear as the disk space became vascularized. Finally, the cord was re-inspected and was seen to lie quite normally in the spinal canal with no further evidence of pressure from an extradural mass. The dura mater was sutured and the rest of the wound was closed in layers.

Course. Slight weakness of the legs and a transitory left Babinski reflex were present immediately after operation, but these had disappeared completely by the time ambulation was allowed on the 8th day. When discharged from the hospital, the child showed no abnormal neurological signs; the gait was normal and flexion of the neck was free and painless.

Follow-up roentgenograms 2 weeks after surgery revealed a small amount of calcium re-

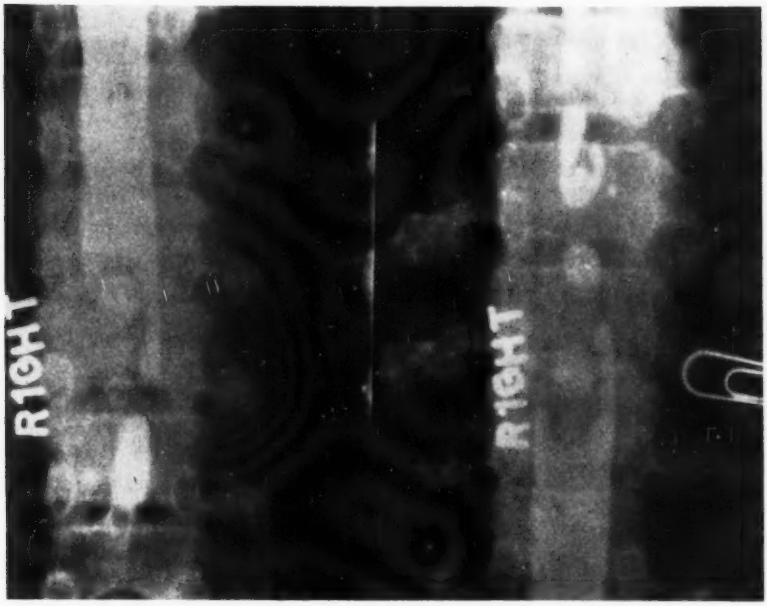

FIG. 3. Myelogram. The dye splits in the midline around the extruded calcium as the patient is tilted up and down.

maining in the interspace but none in the spinal canal. Additional films obtained 2 months later showed further resorption of the remaining calcium. The patient was entirely asymptomatic at this time. At 6 months only a trace of residual calcium was present.

DISCUSSION

The past history of the surgical treatment of herniated thoracic disks is dismal, but recent reports suggest that a more optimistic outlook may be warranted.[1,2,4] Some of the poor results recorded previously undoubtedly occurred in cases in which the patient was brought to operation late with advanced paraplegia.[3] Several technical points in the surgical approach to a diseased thoracic disk bear repeated emphasis. A wide laminectomy is necessary, frequently with sacrifice of a pedicle or two. The dura mater should be opened immediately to determine the level of the rupture and so obviate exploratory extradural procedures which are tedious and sometimes performed at the wrong interspace. Additional mobility of the cord is

gained by dividing nearby dentate ligaments. The disk protrusion is then most safely approached extradurally, using stay sutures in the cut edge of dura mater for retraction of the cord. The herniated portion of the disk is removed and the interspace is cleaned out as thoroughly as possible with small curettes and rongeurs. Care must be used in rongeuring bony ridges; the use of chisels and gouges is not without considerable risk. One may have to be content at times with the decompression produced by division of dentate ligaments, as suggested by Kahn.[2]

Calcification of an intervertebral disk is usually confined to the annulus fibrosis and is generally considered to be a chronic degenerative process of limited clinical significance. Calcification occurring in the nucleus pulposus is less common, and apparently is of greater clinical importance, at least in the thoracic region. Logue[3] cited 11 cases of ruptured thoracic disks with compression of the cord proven by operation, 7 of which showed calcification of the protruded nucleus, and 1 other of a nucleus four segments above the rupture which was calcified. A radiographic study by the same author of 100 other cases at random, in which roentgenograms had been taken because of various local spinal symptoms, revealed only 4 instances of nuclear calcification. Logue concluded that "nuclear calcification in the thoracic region is indicative of a degenerative change of such a nature as to render the disk liable to prolapse." However, in Love and Kiefer's[4] series of 17 cases of protruded thoracic disks only 1 showed nuclear calcification.

A uniform calcification of all the intervertebral disks is seen in alkaptonuric ochronosis, in which there is a defect in the metabolism of tyrosine and phenylalanine resulting in an incomplete breakdown product, homogentisic acid. The latter is precipitated in various avascular tissues, such as cartilage, where certain chemical changes result in the development of a black pigment. The deposits of pigment eventually cause degeneration of the cartilage with metastatic calcifications. This disorder occurs in the fourth and fifth decades and is not associated with calcifications in children.

The calcification that occurs in the nucleus pulposus of children has several distinguishing features compared to those observed in adults.[9] The most striking differences are the transitory nature of the juvenile lesion, the acute local and systemic symptoms that accompany its presence and which often signify its resolution, the relative rarity of its rupture through the annulus, and its similarity to the acute peritendinous calcifications elsewhere in the body.

Characteristically, these nuclear calcifications in children are discovered clinically because of acute local pain and at times an associated mild fever. A traumatic episode a few days before sometimes appears to be the inciting cause of the acute problem, as in Schorr's[6] case and in the present case. It is hardly possible that the dense calcification observed radiologically in these instances, present less than a week after injury, could have occurred in this length of time. It would be more reasonable to assume that the calcification antedated the acute trauma, and that the latter produced an inflammatory reaction with clinical symptoms. This thesis is further substantiated by a case of Silverman's[7] in which previous roentgenograms showed calcification in the disk months before the onset of symptoms. It also corresponds to the natural history of certain other soft-tissue calcifications in the body that are discovered during a painful episode and then are observed to disappear promptly, either spontaneously or after irradiation or partial surgical removal. Follow-up roentgenograms of children with nuclear calcifications have consistently revealed resolution of the calcium over a period of weeks or months.

The transitory nature of these deposits has been commented on by Sandström[5] who has attempted to divide soft-tissue calcifications into two general groups, which he designated permanent and impermanent. Examples of the permanent type are those that occur in the cartilaginous plates and annulus fibrosis of intervertebral disks, in the costal cartilages, trachea and larynx, blood vessels and lymph nodes. The transitory calcifications are found mainly in connective tissue around tendons and joints. He has indicated the microscopic similarities between the connective tissue of the juvenile nucleus pulposus and the peritendinous structures elsewhere, and made the suggestion that the process of calcification in the juvenile disk is similar to that commonly seen in the subacromial region of the shoulder. Indeed, the clinical course of the two are quite alike, and it is interesting to note how quickly the deposits resolve once local blood vessels are allowed access to the lesion. It was striking in the case of the 12-year-old child reported here how similar the toothpaste-like material obtained from the disk was to the material that one encounters in operating on patients with acute calcific peritendinitis of the shoulder, hip or wrist.

Because most of the isolated calcifications of the nucleus pulposus in children do not rupture into the spinal canal, but disappear spontaneously, active surgical measures are not ordinarily indicated. Roentgen-ray therapy carries with it the danger of damage to the epiphyses and is, therefore, probably contraindicated. Stabilization with a posterior spinal support after a period of prolonged recumbency has been advocated by Walker[8] as an appropriate form of therapy. Surgical removal of the lesion should be undertaken when there is evidence by roentgen ray of posterior extrusion into the spinal canal with clinical or myelographic indications of cord compression.

SUMMARY

Calcification of the nucleus pulposus in children is uncommon, usually transient in nature, and at times productive of acute symptoms. Rupture of the calcific material into the spinal canal may occur following trauma and cause compression of the cord, although the more usual course is that of rapid resolution. There are certain similarities, at least in the gross characteristics and clinical behavior, between calcifications of the nucleus pulposus in children and peritendinitis calcarea found in adults. The case of a 12-year-old boy with a ruptured calcified nucleus pulposus in the thoracic region is reported to illustrate these points.

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EPIDERMOID TUMOR (CHOLESTEATOMA) OF THE LATERAL CEREBRAL VENTRICLE

CASE REPORT

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Epidermoid tumors (cholesteatomas) are uncommon intracranial lesions and Cushing reported only 15 examples (including dermoid tumors) in his series of 2,023 verified brain tumors.[2] He did not describe the location of each tumor.

Grant and Austin[3] reviewed the literature in 1950 and reported their series of 22 epidermoids operated upon over a period of 20 years. Fifteen were intradural and were located as follows: 4 in the cerebellopontine angle; 4 near the pituitary; 2 in the third ventricle; 2 in the cerebral hemispheres; 2 in the cerebellar hemispheres; and 1 in the vermis. They cited Mahoney, who in 1936 collected 142 cases from the literature. Of these tumors, 112 were intradural and were located as follows: cerebellopontine angle, 53; parapituitary, 44; and fourth ventricle, 15.

Epidermoids comprise approximately ½ to 1 per cent of all intracranial tumors. Cruveilhier's classic description is well known. His term "tumeur perlée" describes the glistening mother-of-pearl appearance of the outer membrane.

Most authorities agree that the tumor arises from embryonic inclusions of the epidermal portion of the epiblast. They may occur anywhere along the base of the brain from the chiasm to the posterior cistern or may involve the cerebellopontine angle. The extradural lesions may appear in the cranial bones, under the temporal lobes or within the middle ear.[1] The interior of the tumor is entirely avascular and resembles "cottage cheese" in color and consistency.

Bailey[1] described the microscopic structure as follows:

> "On the outside is a thin fibrous layer, within which are flattened epithelial cells which sometimes contain granules of keratohyaline. . . . The central portion is composed of what one might call the ghosts of epithelial cells; their internal structures have disappeared leaving only the shells. This portion resembles the appearance of a dead plant. Besides the skeletons and debris of dead cells one finds some fat and usually crystals of cholesterin."

CASE REPORT

Miss V.D., aged 37, was admitted to Temple University Hospital on Sept. 13, 1955, complaining of progressive loss of vision in the right eye for 3 years. One year before onset of visual impairment, the patient had had "terrific" right supraorbital headaches for 4 months, and none thereafter. Twenty years before admission, she had had generalized convulsions preceded by an epigastric aura associated with a "far away feeling." At that time, an air study done at another hospital was negative. The patient had taken Dilantin gr. 1½ a day for many years. She had had no convulsions for the last 7 years.

Examination. The pupils were equal and reacted well to light. The external ocular movements were normal. The visual fields showed a superior temporal quadrant anopsia on the left with 6/6 vision and a small isle of temporal vision on the right with almost complete blindness in this eye. Fundi showed a pallor of the left optic nerve and atrophy of the right optic nerve. The cranial nerves were otherwise negative. The deep tendon reflexes were hy-

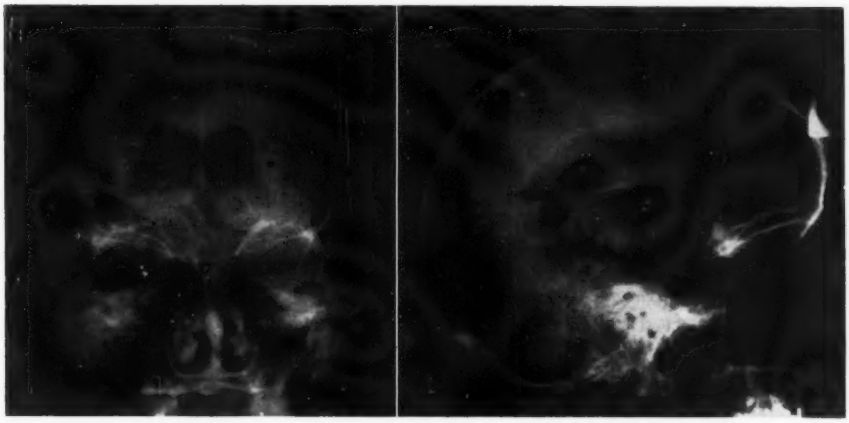

FIG. 1. Air studies showing the "classical" appearance of the epidermoid tumor in the right lateral ventricle.

peractive. There was no Hoffmann or Babinski sign. There was no impairment of sensation, muscle power or coordination.

The laboratory findings, which included complete blood count, sedimentation rate, urinalysis and blood Wassermann, were normal. The electroencephalogram suggested impairment of the left hemisphere, possibly caused by a deep-seated lesion. Roentgenogram of the skull was negative. The spinal fluid contained 1 cell and 50 mg. of protein per 100 cc.; Wassermann and colloidal gold curve tests were negative.

An encephalogram disclosed an irregular cauliflower-like tumor, measuring approximately $7 \times 4\frac{1}{2} \times 4$ cm., occupying the right temporal lobe and ventral horn and actually visualized by the surrounding air (Fig. 1).

Operation. A right temporo-occipital craniotomy was done on Sept. 19, 1955. The dura mater was opened to permit selective herniation of the temporal lobe. A cannula was inserted into the anterior portion of the lobe and it encountered air and slightly turbid ventricular fluid. A horizontal incision was made through the middle temporal gyrus, and an epidermoid tumor was exposed. The white crab meat-like tissue filled the entire right temporal horn up to the body of the lateral ventricle. It was completely removed from the ependymal lining, but a capsule could not be found (Fig. 2). However, when the major portion was removed, a core of tumor was found in the tip of the temporal lobe extending mesialward across the midline of the cranium apparently into the chiasmal area and outside of the 3rd ventricle. This tissue was also removed and a capsule could be seen in the depth of this small finger-like extension. It was thought unwise to strip this capsule because if hemorrhage occurred, it could not be reached through the lateral exposure. However, a small portion of it was removed for biopsy and a silver clip was placed in the area for future identifi-

FIG. 2. Compact flaky tissue removed from lateral ventricle.

FIG. 3. Note silver clip in parapituitary area. This was probably site of origin of tumor before it broke into tip of temporal horn.

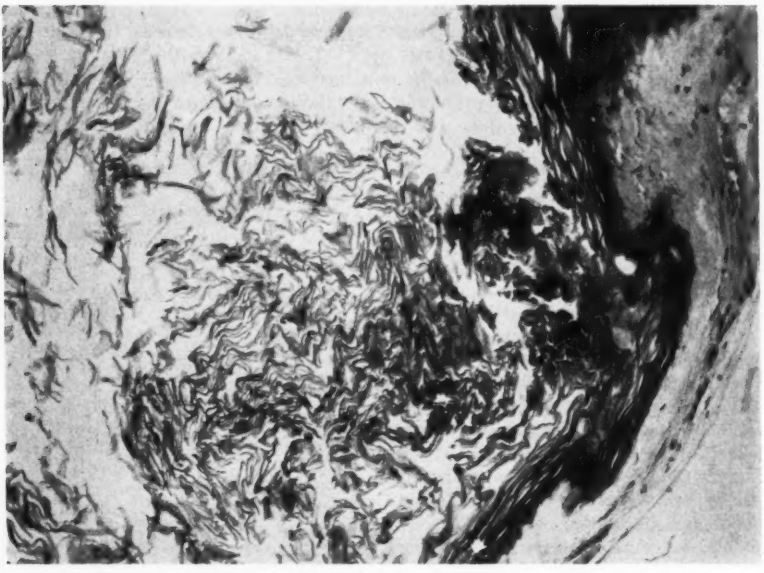

FIG. 4. Photomicrograph of epidermoid tumor. (Hematoxylin and eosin)

cation (Fig. 3). There was no extension of the tumor to the foramen of Monro. The dura mater was closed and the bone flap was replaced.

Pathologic Report. Sections of the cyst wall show a lining of squamous epithelium with keratinous proliferation. Sections of the cyst content show keratinous debris. Diagnosis: Epidermoid inclusion cyst from right lateral ventricle of brain—cholesteatoma (Fig. 4).

Course. The patient made an uneventful recovery. Recent examination showed no change in her visual condition, but she is comfortable and has no complaints.

COMMENT

The clinical course shows clearly that this lesion arose in the prechiasmal parapituitary area on the right, outside of the ventricle, and produced progressive loss of vision in the right eye. The sudden relief of the terrific headaches which were present for 4 months was the result of rupture of the tumor into the tip of the right temporal horn, thus giving the lesion adequate space to expand. The grand mal attacks preceded by an epigastric aura and a "far away feeling" were probably uncinate in nature and caused by involvement of the mesial portion of the temporal lobe.

The classical appearance of the mass in the lateral ventricle as seen in the air studies has been reported as diagnostic of an epidermoid tumor by Hauser and Elkins,[4] who cited similar observations by Krieg, Dyke and Davidoff, Weinberger, Peyton and Baker, and Childe and Young.

The air patterns have been described as irregular streaks, filigree lacework of communicating channels of gas, reticular mass of air, and sponge-like irregular collections of air. Weinberger and also Dyke believed this appearance is explained by the distribution of gas in the folds of the walls of the tumor and that no other known brain lesion produced a similar picture.[4] Lindgren[5] also stated that the epidermoid cholesteatoma is the only space-occupying lesion that gives a typical pneumoencephalographic appearance.

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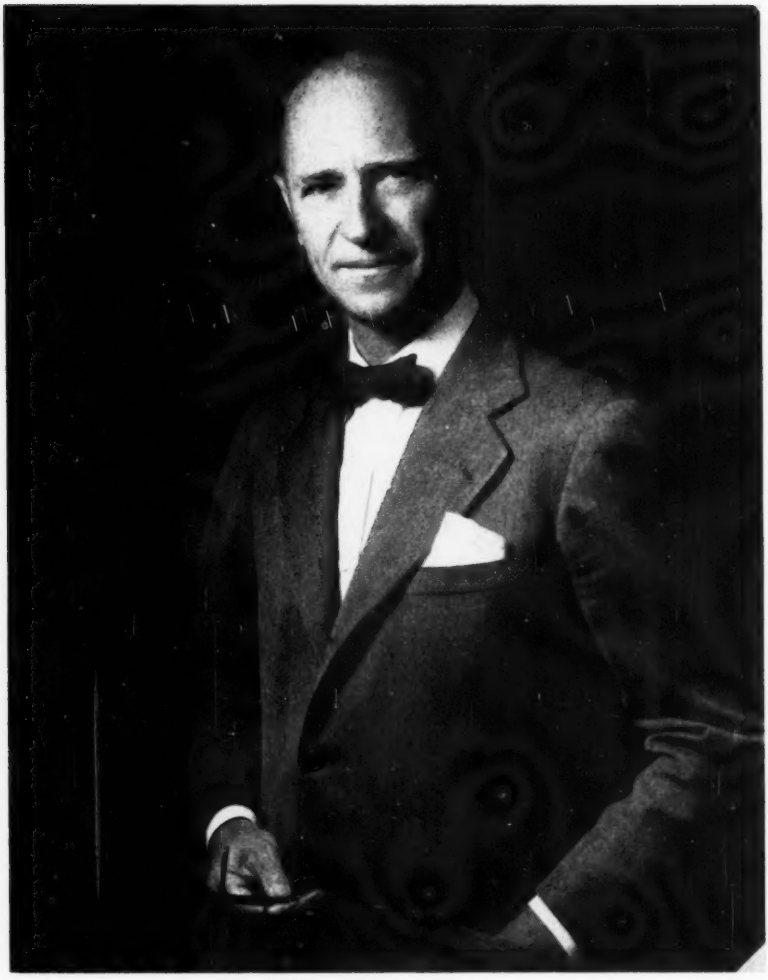
Obituary

ELDRIDGE CAMPBELL

1901–1956



"Im Herzen waechst der Arzt, aus
Gott geht er, des natuerlichen
Lichts ist er.—Der hoechste
Grund der Arznei ist die Liebe."
PARACELSUS

Eldridge Campbell once referred to medicine as the greatest of professions "for by combining the charity which comes from the love of our fellow man with the vast lore of scientific knowledge presently available, we can do much to alleviate the suffering of mankind."[1] Eldridge Campbell's life as physician and surgeon was motivated by this charity to which was coupled an innate strive for scientific progress. This he passed on to those with him and about him as a dedicated teacher. In his personal copy of the History of the Peloponnesian War, he underscored the belief to which he adhered in training and teaching and from which many benefited—

πολύ τε διαφέρειν οὐ δεῖ νομίζειν ἄνθρωπον ἀνθρώπου, κράτιστον δὲ εἶναι ὅστις ἐν τοῖς ἀναγκαιοτάτοις παιδεύεται.[2]

These words of Archidamos illustrate Eldridge Campbell's concept of teaching, a concept that he upheld throughout his professional life.

Eldridge Campbell was born on December 20, 1901, in Alderson, West Virginia, where his father was a country physician. He attended Alderson High School and Randolph Macon Academy. In 1922 he received his Bachelor of Science from the University of Virginia. As a Rhodes Scholar, he attended Balliol College in Oxford and received his Bachelor of Arts in Physiology. In 1927 he was graduated from the Johns Hopkins University School of Medicine. His entire resident training, 1927–1934, was spent at the Johns Hopkins University Hospital. His teacher in neurological surgery was Dr. Walter E. Dandy.

Eldridge Campbell married Eleanor Brown of Baltimore, Maryland, on July 2, 1930. Mrs. Howard Ashby of London, England, Miss Jane Campbell of Loudonville, New York, and Thomas R. B. Campbell, a freshman at Princeton University, are their children.

In 1934 Doctor Campbell joined the faculty of the Albany Medical College, Union University, Albany, New York, and served as Professor of Surgery and Chairman of the Department of Surgery from 1946 until his death. Under his stewardship, Albany Medical College became a foremost Medical Center. His dedication to teaching was reflected in an outstanding resident training program. His creation of the surgical research laboratories enhanced this program immeasurably.

Eldridge Campbell has made fundamental contributions to the neurosurgical literature. His heartfelt interest in the welfare of the individual patient is reflected in his basic writings on management and care of those afflicted with neurosurgical disorders. His strive for scientific progress is mirrored in detailed analysis and studies in the fields of craniocerebral trauma and cerebrovascular pathology, and in neurophysiology. In recent years one of his prime interests was the scholarly translation and commentation of Theodoric's works, the first volume of which he published in his life time jointly with James Colton.

From 1942 until 1946 Doctor Campbell headed the Albany Hospital Unit and was Chief of the Surgical Service of the 33rd United States Army General Hospital in North Africa and in Italy. With the rank of Colonel he served as Neurosurgical Consultant in the Mediterranean Theatre and was decorated with the Legion of Merit. His dedicated interest in military neurosurgery was never more profoundly

demonstrated than during the time in the Korean War when he served as civilian consultant for the Surgeon General. His counsel and assistance in the Korean Theatre were vital factors in the welfare of our neurosurgical casualties.

Recognition has come to Eldridge Campbell from many sides. He was a member of surgical and neurosurgical societies, was founder and first president of the Excelsior Club, and served on the Board of Governors of the American College of Surgeons. During the year before his death, the American Board of Neurological Surgery appointed him Chairman.

Eldridge Campbell's virtues as a man inspired loyal friendship and devotion. The profound impact of his endeavors as a teacher of neurological surgery will be felt for times to come.

ARNOLD MEIROWSKY, M.D.

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BOOK REVIEW

BIOCHEMISTRY AND THE CENTRAL NERVOUS SYSTEM. By Henry McIlwain. *Boston: Little, Brown & Co.*, 1955, illus., 272 pp. Price $9.50.

For neurosurgeons, this book should be an exciting adventure into a new world of thought. The half-sensed, half-seen correlations between chemistry and function of the nervous system are brought into focus in an admirable manner. The author's command of his subject is obvious from the outset. The book is far from light reading, however, neither is it technically clouded beyond the ken of those working on the practical aspects of the nervous system.

After a brief introductory chapter, the metabolism of the brain *in situ* is outlined in 16 pages, including ample references. The following quotable facts are included: The adult human brain, although accounting for only about 2.5% of body weight, receives 15% of the cardiac output of blood, uses 20–25% of the oxygen breathed and about 10% of the glucose in the blood traversing it; its oxygen reserve is sufficient for only about 10 seconds.

The third chapter is concerned with the chemical composition of the brain: The stable and labile constituents, and the inorganic salts in relation to the blood-brain barrier. The following chapter on the metabolism of separated cerebral tissues is a survey of the now extensive field of *in vitro* studies. The dynamic aspects of tissue respiration, glucose, glycolysis, the phosphates, ammonia and glutamine, as well as ion transport are stressed.

The next two chapters comprise a fast-moving account of the two great energy-yielding systems: Glycolysis and oxidative phosphorylation. Included are the participating enzyme systems, their reactive rates, the cerebral concentration of the various degradation substances and, for pyruvate oxidation, the free energy changes. These data are summarized in two excellent tables.

Chapter seven concerns amino-acids and cerebral activities. Major emphasis is on glutamic acid, which with its amide accounts for about 80% of the free α-amino-nitrogen of the brain. Of clinical interest are brief discussions of phenylpyruvic oligophrenia and Wilson's disease.

The following chapter describes the role of the vitamins in the metabolism and function of the central nervous system. This serves to consolidate discussions of the vitamins in previous chapters in relation to the specific metabolic processes in which they play such an important part.

The next chapter is devoted to the cerebral lipids, which comprise about half the dry weight of the brain. Although the early chemical studies of the brain were devoted in large part to the lipids, this difficult subject has only recently gained new momentum. It is these recent developments that are emphasized.

The chapter on cytochemical and histochemical aspects is especially valuable in bringing together the highly important developments in this rapidly expanding field. The dynamic nature of this chapter is well exemplified by the excellent Table 27 in which chemical constituents and activities of specific cellular components are summarized.

Chapter eleven is an interesting account of the variations in chemical and enzymatic make-up of the brain during various stages of development. This is followed by a consideration of the transmitting agents, especially acetylcholine and sym-

pathin. Next comes a discussion of depressants and excitants of the central nervous system. Included is an unique experiment by the author in which electrical stimulation was applied to sections of mammalian brain respiring *in vitro* and the resultant respiratory increase was determined. The addition of an anticonvulsant, Tridione, increased selectively the threshold for this response in the frequency range 500 to 2000 cycles per sec.

The final chapter, although only four pages in length, seems to point a prophetic finger toward the future. It is primarily concerned with the speed of chemical changes in the brain but it is also a preliminary attempt at a trial balance of the thermodynamics of the nervous system. Of the 12 cal./g./hr. energy expended by the brain, it is estimated that a large proportion is devoted to maintaining the differential distribution of sodium and potassium ions; a great amount of the remaining energy is devoted to the metabolism of the substances concerned with transmission and to the renewal of the metabolic machinery of the cells. It is somewhat surprising to learn that the brain's reserve of many essential substances is extremely limited.

The author, Professor of Biochemistry in the University of London, has assembled a vast amount of material in about two hundred pages of text. Much more than a single reading is required for a true understanding of the subject. However, the rapid progress now occurring in this field indicates that those of us who are in the clinical fields had better make a start immediately or be forever left behind.

W. J. GERMAN, M.D.

NOTICES

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AMERICAN ACADEMY OF NEUROLOGICAL SURGERY AWARD

The Second Annual Award of the American Academy of Neurological Surgery was presented to Dr. Hubert L. Rosomoff of Bethesda, Maryland, for his paper entitled "Hypothermia and Cerebral Vascular Lesions. II. Experimental Middle Cerebral Artery Interruption Followed by the Induction of Hypothermia."

The Academy announces its Third Annual Award. Details concerning manuscripts and eligibility of candidates may be found in this *Journal* (1956, *13:* 221).

The recipient of the Third Award will present his paper at the 19th Annual Meeting of the Academy at The Cloister, Sea Island, Georgia, November 11–13, 1957. His expenses while attending the meeting and his travel expenses to and from his home (if living outside the North American Continent, from the port of entry into the United States) will be borne by the Academy. In addition, there will be an honorarium of one hundred dollars.

Manuscripts to be considered by the Award Committee should be sent to Dr. Eben Alexander, Jr., Bowman Gray School of Medicine, Winston-Salem, North Carolina, before July 15, 1957. A resume of the candidate's postdoctoral training must accompany the paper when submitted.

ELDRIDGE CAMPBELL SURGICAL RESEARCH FUND

The Albany Medical College of Union University announces the formation of a Surgical Research Fund in tribute to and in memory of Dr. Eldridge Campbell, gifted surgeon, scholar, teacher and investigator.

Any donations from Dr. Campbell's friends and admirers will be gratefully received by the Albany Medical College.

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It is proposed to commemorate the occasion by holding an International Congress on the Circulation from June 3 to 7, 1957, in the Royal College of Surgeons, London. The range of subjects covers every aspect of the circulation and distinguished speakers from England, France, Germany, Scotland, Switzerland, Sweden, Canada and the United States have already agreed to take part. Further particulars may be obtained at any time from the Honorary Secretary, Dr. D. Geraint James, 11 Chandos Street, Cavendish Square, London, W.1, England. A complete program giving details of both the scientific and social activities will be available in the near future.

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Society of Neurological Surgeons, St. Louis, Mo., May 17–18, 1957. Dr. Bronson S. Ray, 525 East 68th St., New York 21, N. Y., Secretary.

Southern Neurosurgical Society, Nashville, Tenn., March 15–16, 1957. Dr. C. D. Hawkes, 22 N. Manassas St., Memphis 5, Tenn., Secretary.

JOURNAL OF NEUROSURGERY

The *Journal of Neurosurgery* is devoted to the publication of work relating primarily to neurosurgery, including studies in clinical neurophysiology, organic neurology, ophthalmology, radiology and pathology. Short articles on unusual cases and on technique, special instruments or equipment that might be useful to others in the field are also acceptable.

MANUSCRIPTS are accepted with the understanding that they are contributed solely for publication in this *Journal*. They should be addressed to Dr. Louise Eisenhardt, 333 Cedar Street, New Haven 11, Connecticut, U.S.A. They should be typewritten in double space, with tabular matter and passages for small print on separate sheets. All materials should be mailed flat.

REFERENCES should be arranged alphabetically and cited by superior numerals in the text. The following order should be used:

Articles: Name of author, full title of article, name of periodical, year, volume, first and last page of article. Abbreviations of names of periodicals should conform to the style used in *World list of scientific periodicals published in the years 1900–1950* (London: Butterworths Scientific Publications, 1952).

Books: Name of author, full title of book, city, publisher, year, edition, full pagination (if book is in more than one volume, give the number of volumes).

ILLUSTRATIONS. Care should be taken not to use too many illustrations. All figures approved by the Editorial Board are provided free of charge with the exception of color plates, which are inserted at the expense of the contributor. Permission must be obtained from the subject for reproduction of identifiable photographs of patients. If illustrations are larger than 8.5×11 inches, reduced glossy prints should be submitted instead. Any lettering should be large enough to permit necessary reduction. Paper clips should not be used on prints. A hard pencil should not be used in writing on the back of prints. Illustrations should be numbered and the top plainly indicated. Illustrations should be submitted UNMOUNTED.

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HYPERTROPHIC OSTEOSCLEROSIS (BONY SPUR) OF THE LUMBAR SPINE

PRODUCING THE SYNDROME OF PROTRUDED INTERVERTEBRAL DISC WITH SCIATIC PAIN

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(Received for publication June 25, 1956)

THE symptom complex of sciatic pain produced by protrusion of an intervertebral disc of the lower lumbar spine has so dominated our present thinking as to exclude practically all other mechanisms as the cause of sciatica. Mixter and Barr[9] in 1934, Love[6] in 1936, and others, emphasized the importance of the protruded disc as a major cause of sciatic pain. Putti[10] in 1927 first stressed the concept of sciatica being produced by nerve compression in the region of the intervertebral foramen by bony deformities of various types, before the mechanism of the protruded disc was appreciated. Numerous articles have appeared in the literature recently on nerve compression syndrome of the cervical spine produced by bony spurs, whereas little mention has been made of the occurrence of bony spurs in the lumbar spine.[5] An entity of soft-tissue compression in the lumbar area was described by Spurling *et al.*[12] in the syndrome of hypertrophy of the ligamentum flavum as a cause of low back pain in 7 cases. In 6 of their cases mention was made of a noticeable thickening of the overlying lamina at the site of compression. This, we feel, may have been of greater significance than given it by the authors. In the surgical treatment of low back pain and sciatica, one soon appreciates the complexity of mechanisms involved in the production of pain—when after exploratory decompression no adequate cause has been found and yet the patient is relieved of his pain, or when following adequate removal of one or more manifest protruding discs, the patient continues to have pain, not explained by subsequent myelography.

In this discussion, we would like to add localized hypertrophic osteosclerosis (bony spur formation) as another mechanism in the production of low back pain and sciatica as demonstrated in 9 cases. In each instance, the provisional diagnosis was that of a protruded lumbar intervertebral disc. Myelography showed a localized disc-like deformity, that was proved at operation to be a bony spur formation within the spinal canal, compressing the involved nerve root. No disc, hidden or manifest, was found in any case.

ANALYSIS OF CASES

Of a series of 154 patients on whom laminotomy was performed for the lumbar disc syndrome during the years 1952–1955, 9 (5.8 per cent) had localized hypertrophic osteosclerosis (bony spur). The group is too small to

have any statistical value. The 9 cases included 8 females and 1 male whose ages ranged from 30 to 65 years. In a large series of protruded lumbar discs, males predominated 2.1:1.[8]

In cases of actual disc protrusion, the usual mechanism of production is felt to be a flexion or extension stress in which the lumbar spine acts as a fulcrum. Rarely does direct trauma to the spine produce disc rupture. In the group presented here, a fall on the buttock was definitely the common precipitating factor in the symptom complex in 7 of the cases. It is postulated that at the time of the injury, the patient sustained a small fracture or periosteal tear in the region of the interarticular isthmus, with hemorrhage and swelling, producing the initial compression and nerve root irritation with pain. The pain in the back and leg was of immediate onset following the injury in all 9 cases, but it was not as severe and dramatic (ice-pick stab) as occurs in some cases of true disc herniation. The duration of symptoms was from 2 months to 1 year. All patients had fairly severe low back pain together with the sciatic symptoms, but the leg pains were predominant. Four complained of numbness in the involved extremity and 2 of paresthesias. Coughing, sneezing and straining aggravated the symptoms in 4 cases. Three of the 9 patients had fairly good relief on bed rest and another 3 obtained complete relief temporarily, with pain recurring on activity. No permanent relief was obtained in any case by the use of supports and braces or prolonged bed rest, with or without traction.

The findings on examination were typical of those seen in cases of protruded disc, with segmental motor, sensory, and reflex changes, but with 3 notable exceptions. In 6 cases the normal lumbar lordotic curve was maintained and in 3 cases it was lost. In cases of true ruptured disc, the lumbar curve is lost in most instances. Similarly the Soto-Hall test (acute flexion of the neck producing pain at the site of spinal column disorders) was negative in 5 cases, but present in 4, with pain experienced at the site of pressure in the lumbar spine. This test is positive commonly with actual disc protrusion. Thirdly, there was no appreciable body list in any of these cases as is seen frequently with ruptured disc. In this series of bony eburnation the straight leg raising was positive (Lasègue's sign) in 7 cases and absent in 2. Motor weakness was evident in the involved extremity in 4 cases and in 5, motor function was normal. Sensory dermatome deficit was present in all 9 cases. Of unusual interest was the fact that in 8 of the 9 cases, the compressing lesion was of the L5 root at the L4–L5 intervertebral disc level. This produced hypoesthesia over the anterior tibial surface, dorsum of foot and particularly over the great toe. In 1 case the compressing eburnation was at L3–L4 interspace with involvement of the L4 nerve root and hypoesthesia over the lower anterior thigh. Tendon reflexes were normal in 8 of the patients, the one exception being a woman of 65 with a lesion at the L3-L4 level, who had bilateral diminution of ankle jerks, a common finding in the aged. In all cases involvement of the extremity was unilateral and in no instance was the lesion at more than one level.

The first cases were diagnosed erroneously as protruded discs until we learned to correlate the myelographic deformity with the operative findings. In the more recent cases we have learned to suspect the entity of a bony exostosis producing pressure on a lumbar nerve root that resembles so closely the syndrome of a protruded disc.

ROENTGENOLOGICAL FINDINGS

Routine anteroposterior films of the lumbosacral spine were made in all cases. After operating on these patients and reviewing the roentgenograms,

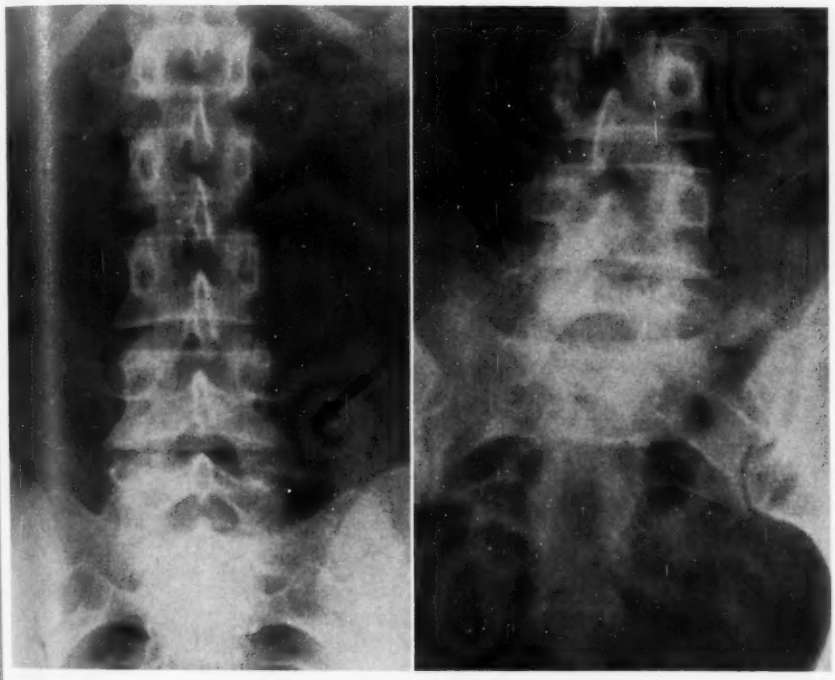

FIG. 1. Anteroposterior view of lumbar spine showing the "bulbous facet."

we have come to recognize that obliquity of the facets at the suspected level is a constant finding. A particular deformity also occurs at the level of involvement. This we call a "bulbous facet." Such a "bulbous facet" occurs at the arthrodial joint on the involved side and is of the anteroposterior type (Ferguson[3]). With this deformity there may be an associated bony spur formation that projects into the vertebral canal which then compresses the nerve root (Fig. 1). If myelography is carried out, the bony spur may not indent the caudal sac sufficiently to produce a deformity although the nerve

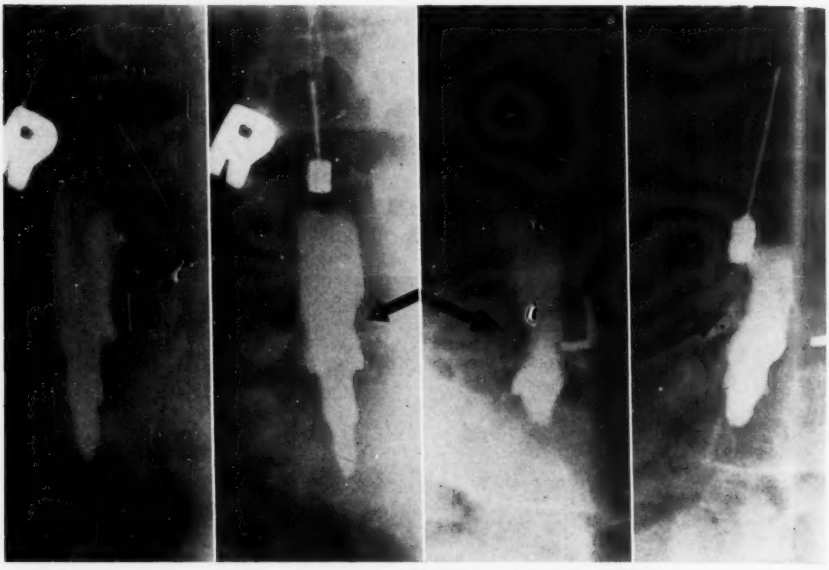

FIG. 2. Pantopaque myelogram, anteroposterior and oblique views, showing large bony spur deformity.

root sleeve may be obliterated since the root is compressed by the bony deformity in its course to the foramen. If the bony spur is larger, it usually produces a concave myelographic deformity that is longer and more smooth than that produced by the usual protruded disc. Similarly, the myelographic deformity produced by a bony spur will be more at a level of the lateral portion of the laminal arch and interarticular isthmus, whereas protruded discs are more likely to occur at the level of the intervertebral disc. By careful comparison of the myelographic defect with the flat film, one will note that the myelographic defect conforms precisely to the medial aspect of the "bulbous facet" that appears to protrude into the lumbar canal (Fig. 2). Unless the myelographic defect is fairly large, the presence of a bony eburnation as the cause of the deformity can only be suspected. However, when the bony defect appears at the precise level at which the neurological findings indicate nerve root compression, then the roentgenographic findings are significant and may indicate a bony eburnation as the probable cause of the compression. An attempt to delineate its outline by special oblique views is most difficult and rarely successful. Myelography is definitely more helpful in oblique views.

In 8 of the 9 cases myelography showed a unilateral defect at L4; in 6 it was manifest, in 1 it was questionable, and in 1 there was obliteration of the nerve root sleeve only. The ninth case demonstrated a typical defect at L3-L4.

TREATMENT

All 9 patients were subjected to a unilateral hemilaminotomy as described by Love.[7] At operation the bony eburnation was found to arise from the medial margin of the facet or adjacent to the facet—the interarticular isthmus, which is that portion of the neural arch where the lamina and the inferior articular facet join the heavy base of the pedicle, transverse process and superior articular facet. This pars interarticularis is felt to be a strategic connecting point in the neural arch and for that reason is subjected to great stresses and strains.[11] As stated by Badgley,[1] "Arthritis of the facets is more

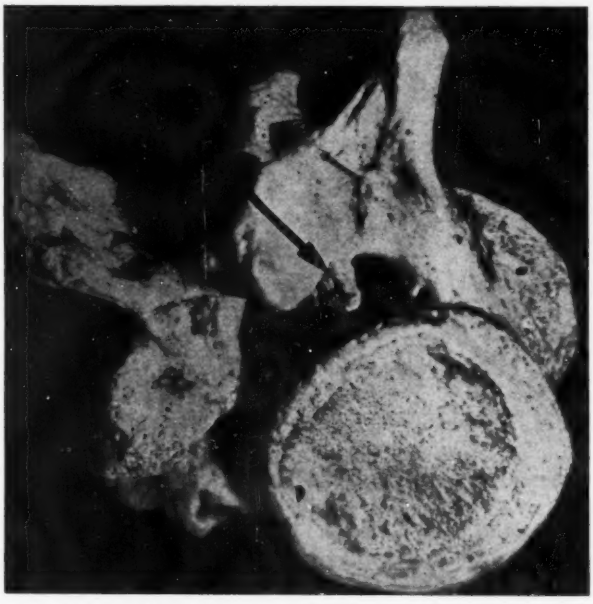

FIG. 3. Hypertrophic osteosclerosis (bony spur formation) of a lumbar vertebra. (Reproduced by permission of Dr. A. Steindler[13] and C. C Thomas, Publisher.)

commonly associated with the asymmetrical facets." Whether this bony eburnation is a degenerative process, a reaction to injury, or a developmental anomaly can only be conjectured. With the history of direct injury to the lumbar spine in 8 of our cases, we feel that the bony eburnation (hypertrophic osteosclerosis) may be a manifestation of traumatic arthritis.

It is noteworthy that in 8 of the 9 cases, the bony spur formation occurred at the L4–L5 level. This is attributed to the fact that the greatest mobility of the lumbar spine occurs at this joint and so it is most easily injured by trauma. Badgely,[1] in a discussion of the facet syndrome, pointed out that "Intervertebral arthritis is more common between L3–L4 and L4–L5 lumbar vertebrae and a little less common in the lumbosacral region itself."

In 3 of the cases the lamina of L4 was so wide as to make access into the canal between the L4–L5 interlaminar space very difficult. In performing a laminotomy at the lateral aspect, the bony lamina was found to be so thickened that visualization of the nerve root coursing beneath it was very difficult. Great care had to be exercised, therefore, by dissection with a small periosteal elevator and cotton patties, so as to avoid injury to the nerve root sheath with a Kerrison punch. In 2 instances the nerve root was found encased within a bony tunnel, and was compressed by this bony exostosis. In 5 cases the exostosis was found to be an elongated bony spur protruding into the dorsolateral aspect and in the longitudinal axis of the canal, causing compression and deviation of the nerve root within the spinal canal (Fig. 3). In 2 of these cases there was a hypertrophied ligamentum flavum adding to the compression, as described by Spurling *et al.*[12] The ligamentous hypertrophy was limited to the area about the bony exostosis. It was necessary to perform a hemilaminectomy in these 2 instances in order to relieve the pressure adequately from the nerve root. It is our impression that any hypertrophy of the ligamentum flavum that may be present is secondary to the pressure and irritation produced by the bony eburnation and is not itself the primary cause of the pressure. In 1 case the major bony exostosis arose from the posterior lip of the upper margin of the vertebral body (L5) adjacent to the pedicle and compressed the nerve root exactly as does a protruded disc. This exostosis was removed by means of a sharp curette. Spinal fusion was done in only 1 case, by an orthopedic surgeon. Neither facetectomy nor foraminotomy were done in any of the cases as the foramina were not obstructed. Extradural venous bleeding was a problem in most cases, because of engorgement from pressure and adhesions about the nerve root and dura mater. No protruding or extruded or "hidden" discs were found in any instance. Operative closure and postoperative care were the same as in cases of protruded discs. Patients were out of bed in 7 to 10 days and were provided with a well-fitted lumbosacral support.

RESULTS

Since the mechanism of pain production is that of nerve root irritation and/or compression, similar to that of a protruded disc, the postoperative results are comparable. There were no deaths. In 1 case a postoperative thrombophlebitis developed in the involved leg that cleared up but with a residual feeling of heaviness of the leg. Eighteen months later the patient fell crossing a railroad track and re-injured her low back. She is the one patient on whom a fusion was performed and she is back under the care of the orthopedist. She has no pain in the leg. Two patients had a temporary residual numbness in the involved leg and foot, 1 for 2 months and the other for 9 months. Two patients had recurrent back pain (spasm), relieved by support, but no pain in the leg. The remaining 4 patients made a rapid and complete recovery. The 9 patients have been followed from 4 months to 3 years. Eight of the 9 have returned to full activity (89 per cent). Of special

interest was the relief of back pain in these cases compared to the persisting back pain that frequently follows removal of an intervertebral disc. It is our impression that even though these patients with a bony spur show asymmetry of the facets with a "bulbous" type of facet at the site of the nerve root compression, but with little loss of lumbar lordosis, postoperatively their lumbar spines are more stable than those of patients who have had a ruptured disc removed.

DISCUSSION

The concept of the protruded intervertebral disc has become so closely associated with the sciatic syndrome that other less frequent localized root-compressing lesions in the lower lumbar area are being overlooked or are not given proper consideration. It seems quite likely that in some reported cases of "hidden disc" the removal of a bony eburnation necessary to uncover the nerve root inadvertently removed the pathological lesion and since no actual disc protrusion was demonstrated it was considered to have been a negative exploration. Since the bony spur lies adjacent to the articular facet, it may be that the syndrome of hypertrophic osteosclerosis we are describing is analogous to the "facet syndrome" first described by Ghormley.[4] In our 9 cases the bony compression did not encroach on the intervertebral foramen and so foraminotomy was not necessary. Neither was it necessary to interfere with the facets' interarticular surfaces to accomplish decompression of the involved nerve root. The bony ridge that is compressing the nerve root directly appears to be associated with a general thickening of the entire lamina of the L4 vertebra with occasional associated hypertrophy of the ligamentum flavum. The composite no doubt adds to the compression phenomenon, but the bony ridge so directly compresses the nerve root sheath as to appear to be the primary factor.

Just how the bony exostosis comes to be formed in that location within the spinal canal can only be speculated. On its operative removal it is usually less rigid and less hard than normal bone. On microscopic section the bone consists of large irregular bone trabeculae, much thicker than normal, with irregular outlines. The cement lines are everywhere well preserved, retain their usual curved appearance and are laid down in parallel lines. There are very few osteocytes in the center of the bone trabeculae. No active proliferation of osteoblasts is seen on the border of the trabeculae nor is there evidence of absorption by osteoclasts. The marrow spaces are rather small and contain only a scanty amount of fibrous tissue. Epstein and Davidoff[2] consider it to be an osteophyte of arthritic origin and mention its removal in 2 young adults with good relief of symptoms. In this small series of 9 patients, 7 had a definite history of a direct injury to the lumbar spine (jarred by sitting down hard). We feel the bony exostosis is of traumatic origin with a periosteal tear or fracture at the interarticular isthmus of the L4 vertebra and the osteophyte forming subsequently. Therefore, the bony spur formation found in these cases may be a form of traumatic arthritis.

In the operative removal of the bony lesion, care must be used to prevent injury to the adjacent nerve root as well as to the facet joint. In the absence of a manifest protruding disc, the disc space should not be penetrated. The question of fusion should be determined by the usual criteria.[14] The results have been extremely gratifying by simple removal of the bony deformity in 8 of the 9 cases.

SUMMARY AND CONCLUSIONS

1. Hypertrophic osteosclerosis (bony spur formation) within the lumbar spinal canal has been demonstrated as another cause of sciatic pain, in the absence of a protruded disc.

2. Nine cases are presented in which a direct injury (with a fall on the buttock in 7 cases) was felt to be the mechanism of production of the osteophyte formation causing pressure.

3. The clinical picture is similar to that of the protruded disc syndrome, less dramatic in its onset but just as persistent in its manifestations.

4. The flat roentgenogram showing a "bulbous facet" at the site of nerve root compression leads one to suspect the presence of a bony exostosis. Lumbar myelography can verify the bony deformity in many instances. We have been unable to find any such lesions described in the current literature of myelography.

5. Hemilaminotomy or partial hemilaminectomy with removal of the bony exostosis relieved the symptom complex completely in 8 cases.

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PATHOLOGICAL LAUGHTER*

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THE relationship between spasmodic, abnormal movements of emotional expression and organic brain disease appears sufficiently interesting to prompt the following review and report of an additional well-documented example of this phenomenon, with its detailed pathologic description.

PREVIOUSLY RECORDED EXPERIENCE

Group I. Case studies documented by autopsy examination offer the strongest evidence of association of abnormal laughter with organic brain disease. Two of the most striking cases studied are those of Foerster and Gagel[13] and Martin.[16] In the former case removal of a papilloma of the choroid plexus was attended by bleeding into the 3rd ventricle. As the surgeon wiped the blood from the space the patient broke into laughter, joked, and was mirthful. The expression responded to repeated mechanical stimulation and ceased each time the manipulation was stopped. At death the ventricle was filled with blood. Martin's case was that of a 25-year-old man who laughed uncontrollably at the grave of his mother during the burial services. Following several recurrent attacks the man was found dead in bed. At autopsy an aneurysm of the termination of the basilary artery was found to extend vertically into the interpeduncular space, compress the corpora mammillaria, and elevate the anterior part of the floor of the 3rd ventricle. An equally notable case presented by Dott[7] concerned an $8\frac{1}{2}$-year-old girl without hydrocephalus who died with an astrocytic tumor that involved the corpora mammillaria and part of the floor of the 3rd ventricle and expanded into the interpeduncular fossa. She had suffered from frequent seizures during which a long aura of uncontrollable and meaningless laughter was always noted. The question as to whether laughter may constitute the aura or the convulsive phase of an epileptic discharge or act as an epileptic equivalent has been discussed by Marchand and de Ajuriaguerra.[15]

Among the autopsied cases of basilary artery occlusion reported by Kubik and Adams,[14] it was noted that some of the patients had shown occasional pathological laughter and crying. The association of laughter in the prodromal stage of hemiplegia was documented by the autopsy findings on a 68-year-old woman as reported by Badt[2] who found bilateral lesions in the pons, caudate nucleus, putamen, and internal capsule.

Cairns[6] described a patient with a large spongioblastoma multiforme of

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the pons without hydrocephalus who, each night, would cry, laugh, and make a noise like a dog. The attacks would last 5 minutes and, at times, consisted of piercing screams followed by laughter.

Davison and Kelman[10] presented 33 examples of patients who exhibited pathologic laughing or crying and who were subsequently studied by autopsy examination. Although cortical and brain-stem lesions were encountered, the majority of the lesions in these patients were in the diencephalic or corticodiencephalic areas. There was no uniformity to the pathologic processes involved, however, since examples of degenerative, demyelinating, neoplastic, and vascular occlusive disease were also found.

Group II. Case studies in which confirmation of the exact location and nature of the lesions is lacking are less convincing, but pertinent. Féré[12] noted 2 cases of 64-year-old patients in which abnormal laughter preceded the onset of hemiplegia. In 1927 Badt[2] recorded a case of a 24-year-old man in which the occurrence of abrupt, short-lived laughter was the prodrome to collapse and a right hemiplegia. A similar case was reported by Martin.[16] The latter author reported 2 additional cases of young people in which laughter preceded a probable attack of subarachnoid hemorrhage in one and death from an unconfirmed upper brain-stem lesion in the other. Clarke[8] presented the case of a 25-year-old patient with a probable basilar artery aneurysm in which hilarity was the early and only symptom.

Group III. The occurrence of emotional lability as evidenced by laughter, crying, and weeping, in association with single hemiplegia, double hemiplegia, pseudobulbar palsy, disseminated sclerosis, amyotrophic lateral sclerosis, and generalized arteriosclerosis, needs no emphasis.[16,18]

Group IV. Although the present discussion deals with facial movements as a part of the phenomenon of laughter, there are facial movements that occur from brain-stem lesions which, while not so highly organized as those occurring with laughter, may be pertinent to the subject under discussion. Abnormal movements of the face in the form of occasional fibrillary twitchings were noted by Pilcher[17] in a patient with a spongioblastoma of the pons. Alpers and Yaskin[1] described the attacks of a 19-year-old woman who had a glioma that invaded the collicular area, floor of the 3rd ventricle, posterior colliculi, 3rd nerve nuclei, posterior commissure, and pulvinar. During each attack, which lasted 3 to 4 minutes, the right side of the face drew up and the right eye closed. It is to be recalled that Cushing[9] reported facial twitching in association with tumors of the acoustic nerve. His Case XXII was that of a 30-year-old man who, for 9 years, suffered left facial twitchings so pronounced as to lead to the diagnosis of focal epilepsy.

Edwards and Paterson[11] recorded facial spasm caused by tumors of the 8th nerve in 17 cases. In 3 of them there was no associated facial weakness.

These examples of abnormal facial muscle movement occurring with brain-stem and diencephalic disease point up the fact that the occurrence of laughter, which involves some of the same musculature, is a separate complex which may utilize the same, final, common pathway, but has a

separate supranuclear organization of electrical discharge. Direct involvement by disease of the nuclei of the nerves that serve muscles of emotional expression is well known and is manifested primarily, if not exclusively, by paresis of function rather than by the abnormal and excessive movements with which we are concerned in this report. Such paralysis may be the end result of a process that had previously been associated with excessive emotional display. Paucity of emotional expression, particularly laughter, is readily observed in patients with paralysis agitans and the parkinsonian syndrome. Evidence of a decrease in emotional display, which is associated with other demonstrated lesions, is afforded by Barnett and Hyland,[4] who reported an example of a marked reduction in hearty, but appropriate, laughter in a patient with a malignant pinealoma that destroyed both colliculi and spread back to compress the vermis of the cerebellum beneath the tentorium.

CASE REPORT

The present case is another example of a patient demonstrating pathological laughter associated with organic brain disease and is documented by a detailed pathological analysis.

R.E.F., a 39-year-old language instructor at the college level, was admitted to the Wadsworth General Hospital, Veterans Administration Center, Los Angeles, on Dec. 31, 1954, with the chief complaint of difficulty in walking and writing. In mid-December 1954, the patient suffered from general malaise over a 2-day period, similar to influenza. At this time, he noted some difficulty with his gait, in that his right lower extremity became weak and he lurched to the right. Likewise, his right hand had the feeling of impaired circulation, and his handwriting gradually became illegible. All other paresthesias were absent. From the onset of symptoms 2½ weeks before admission, the patient complained of bilateral blurring of vision without diplopia, as well as some slurring of speech. A dull, right occipital headache occurred sporadically, and difficulty in starting the urinary stream and occasional incontinence developed throughout this same period. By the time of admission, the progression of symptoms confined the patient to bed; he was unable to walk and complained of rotatory, vertiginous sensations and nausea without vomiting.

Notable in his history was the following: In October 1954, the patient found himself laughing for no apparent reason when in conversation with some undergraduate students. Although he considered this a breach of proper conduct, at the same time he realized that he was unable to stop. By the time the other symptoms had developed in mid-December, this complaint had become noticeable to the patient's mother. The laughter, which was spasmodic and inappropriate, ceased on December 15, but recurred 2 days before hospital admission.

The remaining past, family, and social history was not pertinent.

Examination. The patient's blood pressure was 110–78, and the pulse rate was 78. He was lethargic, but oriented and cooperative. Reasoning was defective, attention span was short, and arithmetical calculations were often erroneous. Significant but mild, resistance to flexion of the neck was noted. Smell was intact, visual acuity was unimpaired, and the fundi and pupils were normal. Upward gaze was defective and limited, a true vertical nystagmus was observed, and upon attempted upward gaze, the right eye abducted. Adduction of the left eye was severely limited. A

mild, peripheral type, right facial weakness could be discerned, the jaw deviated slightly to the left, and the gag reflex was depressed bilaterally. The outstretched right arm drifted mesially, and tone was increased in the right extremities. Coordination was defective bilaterally; the patient would fall to the right when standing, but could walk guardedly with support.

There were alternating variations in the reflexes between the two sides, but the right plantar response was consistently abnormal. Position sense was impaired on the right side.

A striking feature of the examination was the paroxysmal laughter which the patient evidenced at examination on Jan. 1, 1955. The patient had insight into this laughter which interrupted the interview repeatedly every 45 to 90 seconds. The onset was abrupt, almost explosive. He grimaced and laughed a vocal laugh which

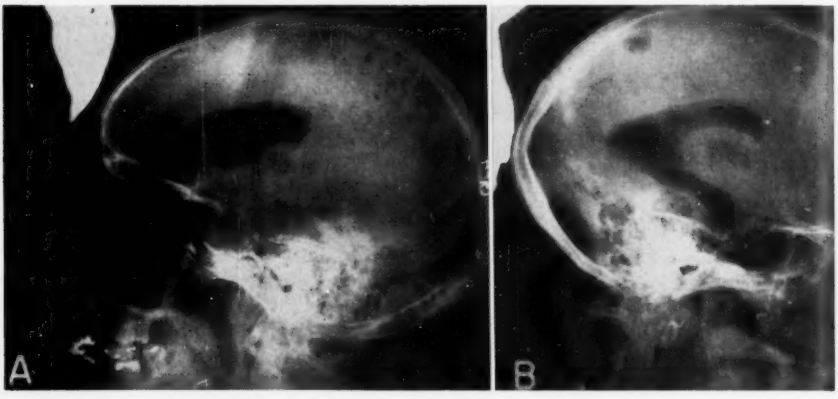

FIG. 1. (A) Brow-up ventriculogram projection to demonstrate mild obstructive hydrocephalus and forward tipping of 3rd ventricle upon its "nose." (B) Brow-down projection to demonstrate obliteration of aqueduct of Sylvius immediately beneath pineal shadow.

seemed mirthless but was certainly a laugh, although more of a stage laugh. Each episode lasted a few seconds, and the laughter disappeared as quickly as it came. It would interrupt a serious sentence, the patient did not talk during it, and he would then resume his sentence in normal context to the conclusion. If asked a question, the patient might laugh prior to answering, but at the completion of the laugh he would answer the question appropriately. There was no crying. The patient said that he could not stop the laughter and that there was nothing funny to his mind about the environment.

In its motor display the laugh was indistinguishable from the "normal" act of laughter; respiratory and facial movements were identical. Although it was not a raucous or loud display, vocalization occurred and, at times, the patient seemed to be chuckling to himself. It did not appear that he suffered any impairment of consciousness during the laughter. Specific tests were not recorded, and by the following day, when an electroencephalogram could be performed, the laughter had ceased.

Subsequent to this examination, there was no recurrence of the abnormal laughter to the time of death, 20 days later.

On the 4th hospital day ventriculography demonstrated a mild, obstructive

hydrocephalus. The 3rd ventricle was dilated, tipped forward on its "nose," and filled with gas backward to the origin of the aqueduct of Sylvius. The upper end of the aqueduct appeared as a tapered point, indicating a total block at this site (Fig. 1). An obstructive lesion in the floor of the 3rd ventricle and the aqueduct of Sylvius was the ventriculographic diagnosis.

Operation. A ventriculocisternostomy was performed on the same day.

Course. By the 8th postoperative day (Jan. 9, 1955) the patient was unresponsive, intermittent temperature elevations to 106°F. (41.1°C.) were noted, and a bilateral extensor rigidity had developed. Both pupils were dilated and non-reactive to light. The right pupil measured 5 mm., the left 7 mm., and subsequently, both pupils assumed a mid-dilated size and remained unresponsive to stimuli. The pulse

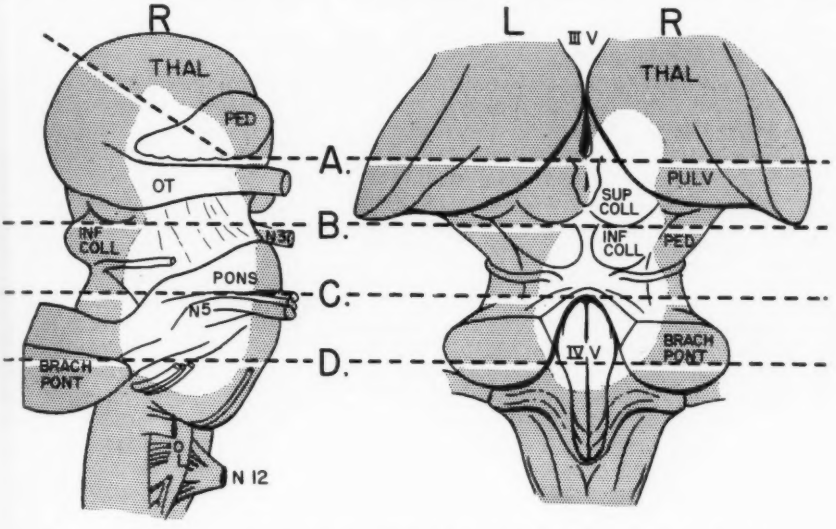

FIG. 2. Two-dimensional reconstruction of the total extent of the lesion in the brain stem. The levels marked A, B, C, D, appear in Fig. 3.

fluctuated from 95 to 135 points and, in spite of careful tracheotomy toilet, the respiration varied from 20 to 30 points. The patient expired on Jan. 20, 1955.

Pathology. At autopsy, except for mucopurulent bronchitis, sphenoid sinusitis, and a minimal generalized arteriosclerosis, the findings were generally confined to the nervous system.

Gross description of the nervous system. There were a few ecchymotic areas in the occipital portion of the scalp beneath which there was a surgical defect in the bone, measuring 1.5×4.5 cm., that extended into the foramen magnum. A small, red rubber tube protruded into the dura mater through the bony defect and entered the cisterna magna. The longitudinal sinus was patent and the bridging veins were free of blood. The under-surface of the dura mater was smooth and glistening, the leptomeninges were thin and transparent, and the cerebral hemispheres were symmetrical and normally developed. The vessels of the circle of Willis were thin and pliable. The cranial nerves were bilaterally intact and, aside from some swelling of the optic

nerves and chiasm, appeared normal. The tuber cinereum bulged inferiorly, distorting the mammillary body on the left. There was some molding of the cerebellar tonsils about the medulla, and the uncus was slightly notched bilaterally, but more so on the right. There was a bilateral "fungus cerebri" noted in the posterolateral edge of the superior parietal lobules corresponding to cranial burr openings.

The pons was greatly widened and the basilar artery lay in a fairly deep groove along the inferior surface. A small mass of clotted blood lay at the anterior edge of the pons just posterior to the 3rd nerve exit and extended into the interpeduncular space. The brain was sectioned coronally. The basal ganglia and the anterior limb and genu of the internal capsules appeared normal. The right lateral ventricle contained a small quantity of fresh blood clot. The great internal cerebral veins and dural sinuses were patent. In the anterior portion of the medial thalamic medullary lamina and medial thalamic nucleus on the right, there was a hemorrhage which measured 0.9×0.5 cm. (Fig. 3A). At this same level on the left was a slight distortion upward of the corpus callosum, its lateral portion traversed by a hemorrhagic

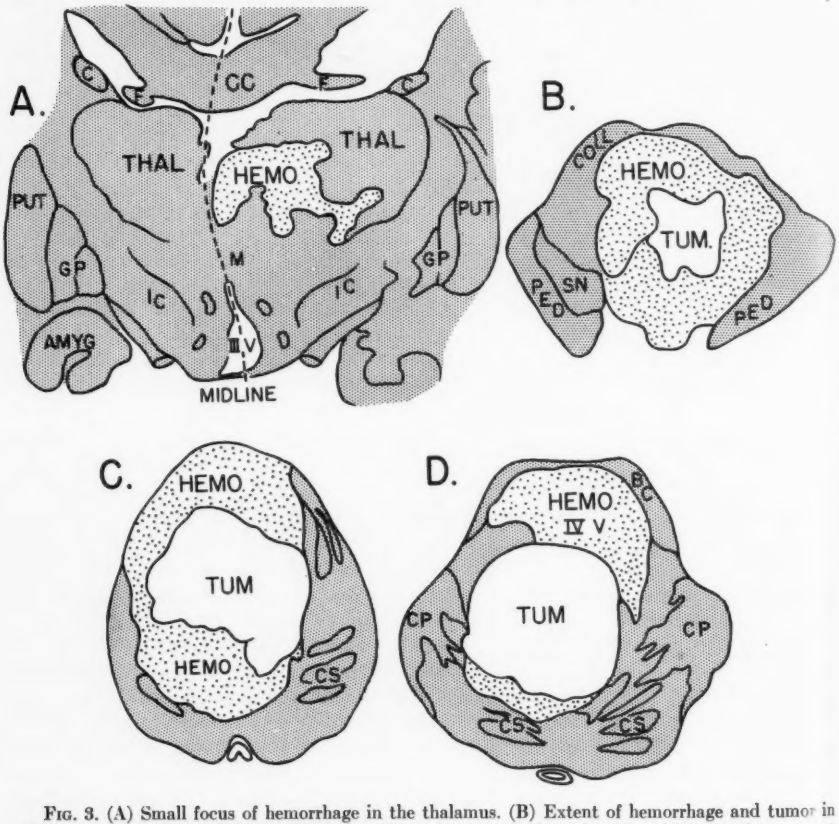

FIG. 3. (A) Small focus of hemorrhage in the thalamus. (B) Extent of hemorrhage and tumor in midbrain. Note loss of red nuclei and of the substantia nigra on the right. (C and D) Showing greatest extent of neoplasm in upper and lower levels of pons.

streak which was continuous with a needle tract projecting inferiorly from the "fungus cerebri" on this side. The 3rd ventricle was stained by a small quantity of blood. In serial section between Figs. 3A and 3B, the entire right thalamus, except for the lateral portion of the lateral nucleus, the substantia nigra, and the red nucleus, was hemorrhagic. The right peduncle was markedly compressed. The pineal gland was shifted somewhat to the left and compressed against the inferior surface of the splenium. Hemorrhage and a small sharply circumscribed nodule of gray tumor tissue occupied all of the structures of the mesencephalon, except for a thin periphery (Fig. 3B). The peduncles were markedly thinned. The body of the pons was occupied by a tumor mass surrounded by hemorrhage (Fig. 3C). The hemorrhage extended into the aqueduct and 4th ventricle and depressed the tumor inferiorly. The corticospinal tracts in the pons were markedly compressed but espe-

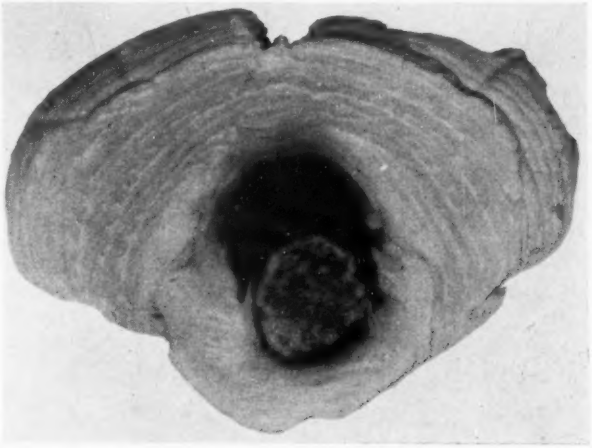

FIG. 4. Photograph of gross lesion in section between Fig. 3C and 3D. Note circumscribed white tumor mass surrounded by rim of hemorrhage. The hemorrhage also fills the 4th ventricle.

cially so on the left (Fig. 3D). The lowest levels of the pons contained clotted blood in the centrum but no apparent tumor. There was filling of the 4th ventricle and compression of the dentate nuclei (Fig. 4). The medulla was markedly swollen. The ependyma of the posterior 4th ventricle and the foramina of Luschka were blood-stained. A reconstruction of the lesion in the brain stem is shown in solid form in Fig. 2.

Microscopic description of the central nervous system. Sections were taken at 5 mm. intervals throughout the entire brain stem and representative areas of the cerebrum. These sections were then studied with hematoxylin and eosin and Weil preparations.

Cerebral cortex: Sections taken from frontal, temporal, parietal, and visual cortex showed no abnormalities, except for changes in the posterior aspects of the superior parietal lobule incident to ventriculostomy.

Diencephalon: The hemorrhage noted grossly extended through the right medial thalamic nucleus, medial thalamic medullary lamina, lateral thalamic nucleus, and into the edge of the massa intermedia. The hemorrhage compressed the right cere-

bral peduncle and internal capsule, causing small bubbles and swellings in some myelin sheaths on the right. There were a few gitter cells and an occasional tumor cell seen in tissue nearest the peduncle.

Mesencephalon: Only a thin rim of tissue remained of the midbrain: the left peduncle was morphologically intact. The right peduncle had some scattered focal demyelination. The nucleus of the 3rd nerve was destroyed bilaterally, and the destruction extended into the lower edge of the midbrain and damaged the 3rd nerve tract as well. The substantia nigra was intact on the left but destroyed on the right. The red nucleus was destroyed bilaterally (Fig. 3B). There were small islands of bizarre tumor cells scattered through masses of hemorrhage in the centrum of the mesencephalon. The aqueduct could not be identified.

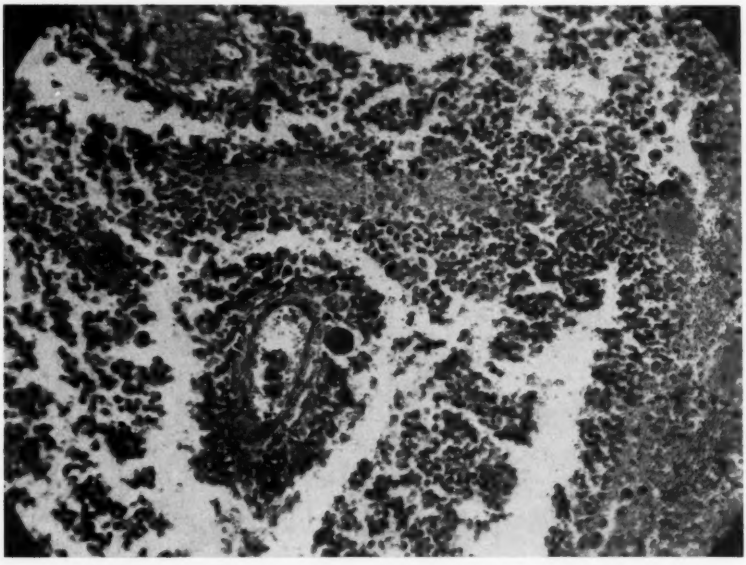

FIG. 5. Microphotograph of the neoplasm showing the perivascular arrangement of cells and variation in size, shape, and staining characteristics.

Pons: The basilar artery appeared normal. The entire centrum of the pons was occupied by a sharply circumscribed tumor mass surrounded by a thin film of hemorrhage. The corticospinal tracts were compressed bilaterally, but more so on the left. The tumor extended through the tegmentum and obliterated the cephalad portion of the 4th ventricle. At the level of the 5th nerve, the tumor mass occupied the centrum but slightly to the left side and more basilar than in the upper levels (Fig. 3D). Hemorrhage filled the 4th ventricle, and surrounding the tumor there were myriads of gitter cells. The tumor was best examined at this level. The cells were bizarre in outline, varying from cuboidal to hexagonal with varying shapes and depths of staining. The nuclei were oddly shaped and deeply stained. There were scattered mitoses seen. Some cells were giant in form with stellate spicules at the edges. Some contained small granules of pigment. Many cells formed thick cuffs around blood vessels (Fig. 5). Other areas revealed fronds, but there were no pave-

nent cells seen. Tumor tissue was no longer seen at the lower edge of the pons.

Medulla oblongata: The taenia choroidea near the lateral recess housed a number of small islands of normal-appearing ependymal cells and canal-like structures which streamed into the superior aspect of the acoustical eminence. There was a small mass of tumor in the 4th ventricle, actually an extension posteriorly of the main tumor mass and not attached to the floor of the 4th ventricle. The neuroglia were markedly increased throughout the acoustic and hypoglossal nuclei.

Cerebellum: No remarkable changes were noted.

Spinal cord: Sections through all levels of the spinal cord revealed no abnormal findings.

The tumor was malignant and ultimately thought to represent an example of metastatic melanoma, although extensive search failed to reveal any focus of a primary lesion.

COMMENT ON CURRENT CASE

The patient whose history we have presented apparently did not experience any change in his affect or emotion that corresponded to overt demonstration of hilarity or humor, viz laughter. The display, admittedly of short duration and not fully documented, did appear to reflect a corresponding mood superficially; but it lacked the warmth of autonomic display that one associates with mirthful laughter. In this respect, we do not agree with Wilson[18] who wrote that the pathological emotional state is, in quality, identical with normal emotion; but we do agree that the "body reverberation is not *per se* the emotion." We also agree with Martin[16] that what is observed in this type of case is merely the hollow, external manifestation of mirth.

It is germane to this discussion to note the observations of Brown[5] from his work on the male chimpanzee after decerebration in front of the anterior colliculi. He stimulated the exposed surface of the caudal half of the brain stem in the central gray matter around the aqueduct of Sylvius, 1 mm. from the midline and 3 mm. below the posterior commissure. An alteration in respiration was produced akin to a chimpanzee laugh. Brown considered the act of laughter, in large part at least, as an alteration of the act of breathing. There was no "conditioning of the emotion associated with the reaction of laughing." The rage evoked by Bard[3] in experimental animals occurred after removal of all parts of the brain cranial to the middle of the diencephalon and after removal of the dorsal part of the thalamus. If the ventral and caudal portions of the diencephalon were separated from the midbrain, the exhibition of the sham rage did not occur.

We think a distinction may be made between two groups of patients, both of whom are afflicted with uncontrollable laughter. One group consists of those patients in whom one may observe an excessive emotional display (characterized by frequent, uncontrollable, inevitable and, therefore, pathological outbursts) which, at the same time, is associated with feeling or true emotion, even though this emotion may, at times, seem contradictory in the relationship of cause and effect. This is often caused by a disease that removes cortical inhibition and results in a release of effective response that de-

pends upon the integrity of the diencephalon and the brain-stem motor connections. The second group consists of those patients in whom there is no recognizable stimulus to emotional display nor emotion experienced during the overt demonstration of laughter, save possibly the surprise at its occurrence. We believe our patient belongs in this latter group.

It was the abnormal discharge of a system that controlled the muscles of emotional expression (and their closely allied respiratory muscles) without accompanying "feeling tone" that our patient exhibited. This mechanism is characteristic of most other cases of associated pathological laughter and circumscribed disease of the upper brain stem and diencephalon reported in the literature. We are not able to say whether our patient was able to express true emotional experience in the same overt fashion. This would have been interesting since, if the expression of emotion had been paralyzed, we would have had evidence of the interruption of the diencephalic influence on the expression of emotion in the face of an abnormally excitable and, at times, partially paralyzed (partial 7th cranial nerve paresis) corticobulbar system. It is worth noting, however, that the abnormal discharge did not result in movements other than those usually seen with laughter. There was no massive excitation nor spread of abnormal innervation.

The episodes of laughter were abrupt in onset and cessation and of short duration, dominating all other activity. They were similar to an epileptic attack, although the patient was aware of their occurrence and quality and, insofar as bedside analysis could ascertain, was not amnesic or out of contact. It is tempting to postulate a phase of excitation in a system which controlled emotional expression in this specific way. Following such a period of episodic stimulation, there may have ensued the paralysis of this system with the resulting cessation of laughing attacks and the rapid development of midbrain dissolution. The hemorrhage which was found to occupy so much greater an area than the tumor itself was of recent origin and, timewise, conceivably occurred when the patient became comatose and decerebrate on his 8th postoperative day. The illustrated extent of the tumor tissue itself gives a truer picture of the state of the lesion at the time laughter was occurring and is the more important map for anatomico-physiologic correlation.

Our anatomical contribution is not discrete and permits little more than speculation. We considered it worth while, however, to add this case to the growing number that illustrate a relationship between abnormal laughter and organic disease of the brain stem and diencephalon.

SUMMARY

A review of previously recorded experience with cases involving abnormal emotional expression and organic brain disease has been presented.

An example of the association of an upper brain-stem and diencephalic neoplasm with attacks of abnormal laughter has been studied. A diencephalo-mesencephalo-integrating system responsible for emotional expression may

have been stimulated and subsequently paralyzed by the advancing tumor. A distinction may be made between disease processes that act by interfering with cortico-diencephalic influences on such a system and processes that, like the example presented, primarily affect the system locally with an epileptic-like discharge.

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ADDENDUM

Since acceptance of this manuscript, the following two articles dealing with aspects of this subject have appeared:

1. Druckman, R., and Chao, D. Laughter in epilepsy. *Neurology*, 1957, *7:* 26–36.
2. Ironside, R. Disorders of laughter due to brain lesions. *Brain*, 1956, *79:* 589–609

ACUTE HEMORRHAGE INTO PITUITARY ADENOMAS

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HEMORRHAGE into a normal pituitary gland, with or without later signs of hypopituitarism, is said to occur in many conditions.[15,18–20,25,32] Kraus cited reports of pituitary hemorrhage in anencephaly, cretinism, cardiac failure, tetanus, erythremia, sepsis, abdominal typhus, miliary tuberculosis, Basedow's disease and diabetes mellitus; he stated that bleeding is found frequently in pituitary tumors. Although this latter complication is well recognized,[19] it can hardly be said to be common. However, it is probably more common than usually is thought, since reports in the last few years are usually of several cases each,[7,14,23,27,34] whereas nearly all the reports before 1949 dealt with isolated instances.[5,8,30,35,37]

A search of the literature uncovered reports of a total of 71 cases of hemorrhage into pituitary adenomas.[1–3,5–11,13,14,16,17,21–23,26–36,38,40–42] The condition in 35 of these cases was acute,[2,3,5,7,9,10,17,21,23,26,28,34–36,41,42] and the hemorrhage in another 13[13,27,33,34,39] was associated with roentgenological treatment, of which bleeding is a recognized complication, although Sosman[39] said it is infrequent. It is difficult to assess the actual incidence but Müller and Pia[27] found 19 instances of hemorrhage in a series of 270 pituitary adenomas; the condition in 3 of the 19 was acute. Müller and Pia classified hemorrhage into pituitary tumors as acute, subacute and chronic; this classification is useful but not completely accurate, since a patient may give a story of one or more subacute episodes before a final acute one;[6,7,23,26,34,35] also, evidence of both old and recent bleeding may be found at necropsy[12] or operation.[7,14,34,38] Acute bleeding is sudden and is accompanied by compression of the chiasm, optic nerves and cavernous sinus[27,41] and also not infrequently by penetration of the capsule of the gland, with subarachnoid hemorrhage. More unusual forms occur so that the picture may be rather misleading, as in the case of Schnitker and Lehnert;[36] although their patient was known to have a pituitary adenoma, the exact diagnosis was not suspected at first because compression of the middle cerebral artery produced the clinical picture of closure of that artery. Other findings to confuse the diagnosis were presented in the third case of Brougham and associates;[7] the patient in question had

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right hemiparesis. Another of their patients had facial pain from compression of branches of the fifth cranial nerve in the cavernous sinus.

In the acute stage of hemorrhage into a pituitary adenoma, the clinical picture must be distinguished from that of a ruptured congenital aneurysm.[9,12,16] Clinically, this may be difficult, especially if the patient is drowsy or in coma. However, when evaluation of the visual fields can be done, the usual defects thus found may be diagnostic of a pituitary lesion. Furthermore, the amount of blood in the cerebrospinal fluid demonstrated by spinal puncture tends to be somewhat less in pituitary hemorrhage than in subarachnoid hemorrhage from an aneurysm, and, of course, there may be none at all. The diagnosis can be made more readily if the patient is known to have a pituitary tumor or is having roentgen treatment for one. Even if this is not so, the patient may show signs of pituitary dysfunction, such as acromegaly,[2,6,9,16,17] as seen in one of our patients, and an adenoma of the pituitary could be suspected. When a tumor is known to exist, the possibility of an acute pressure cone[16] at the tentorial notch or of secondary adrenal insufficiency[23] as a cause of the coma should be considered.

Clinical and laboratory evidence of anterior pituitary insufficiency would be helpful in making the diagnosis of hemorrhage into a previously asymptomatic pituitary adenoma. However, such evidence may not appear with acute episodes and one must rely on the changes in visual fields plus signs of increased intracranial pressure. Patients who have had several episodes of bleeding might well present the appearance of hypopituitarism or show comparatively rapid accentuation of pre-existing signs and symptoms of this condition and one perhaps should suspect bleeding as the cause in such circumstances. Demonstrable pituitary insufficiency during the time of hemorrhage did not occur in either of the 2 cases to be reported.

The diagnosis is helped greatly by evidence of a ballooned sella turcica in lateral roentgenograms of the skull, although this classic roentgenographic picture is not present in all cases.

Sudden death associated with a pituitary tumor without hemorrhage has been reported in several cases.[12,24,26,37] An uncomplicated pituitary tumor might, therefore, have to be considered in the differential diagnosis but such differentiation would be of little practical value in decisions regarding treatment.

PROGNOSIS

Some of the case reports in the literature lack sufficient detail to allow clear analysis of the results. In the acute lesions reported in the past, the outlook has not always been good and the mortality rate has been high. In more recent reports, however, improvement has occurred in morbidity and mortality rates. Of the 35 patients reported on who had acute hemorrhage, at least 21 died of the hemorrhage. Death was instantaneous in some patients, whereas it took place from a few hours to a month after the onset of the symptoms in others. In the remainder, some recovery of vision or of ocular movements or both was noted in at least 9 instances. Recovery of

vision might be extremely rapid, as in Röttgen and Peters'[34] first case, in which vision was noted to improve during craniotomy with the patient under local anesthesia as soon as the blood clot was sucked out of the gland.

TREATMENT

Craniotomy is imperative as soon as the diagnosis can be made. Pressure on the optic nerves, the hypothalamic region and the anterior part of the third ventricle can be relieved only by removal of the blood clot within the bulging capsule of the tumor.

It is our impression that patients undergoing operations on the pituitary tolerate the procedure better if they are prepared adequately by administration of hormones. This is certainly true if the patient already shows signs and symptoms of pituitary insufficiency. These patients preferably should receive cortisone and, in many instances, testosterone or thyroid or both. Even if evidence of hypopituitarism is absent, we prepare the patients with large doses of cortisone given intramuscularly for 2 days preceding operation. Cortisone is usually given in decreasing doses for a few days after operation. Patients who have bleeding into a pituitary adenoma should be treated in the same manner. If surgical intervention is urgently needed, as may be true when the hemorrhage is sudden and large, compound F may be given intravenously during the operation and until such time as intramuscular injections of cortisone attain their effect.

Right transfrontal craniotomy is preferable because of the ease of approach if the surgeon is right-handed and because the right cerebral hemisphere is the nondominant one in the majority of patients. If the patient's general condition will not tolerate general anesthesia, local infiltration of the scalp will suffice. After the optic nerves and chiasm have been exposed by either an intradural or an extradural approach, the capsule of the tumor is incised. Old liquid blood usually fills the operative field. It is unusual to encounter bright red blood. With the use of a sucker, the intracapsular contents are thoroughly aspirated. Extremely small amounts of viable tumor tissue frequently are found, although enough usually is obtained to permit microscopic diagnosis of the type of adenoma. The capsule is resected sufficiently to permit inspection for persistent bleeding points in the base or wall of the capsule; these can be controlled by careful electrocoagulation or by insertion of Gelfoam or a piece of muscle for tamponade. If the opening in the capsule is generous, collections of fluids can gravitate out without producing pressure. Total removal of the capsule is desirable but it increases the risk to the patient.

Recurrent hemorrhage is most unusual. However, in the case of Röttgen and Peters,[34] the hemorrhagic cyst, after being emptied, quickly refilled with blood and the authors suspected they were dealing with an aneurysm. If the presence of an aneurysm is suspected, it would be propitious to insert a spinal-puncture needle of medium caliber into the cystic mass prior to direct incision of the capsule. If bright red blood trickles from the needle or

is obtained by gentle aspiration, the possibility of an aneurysm must be strongly suspected and the advisability of capsular incision should be carefully reconsidered.

REPORT OF CASES

Case 1. A 64-year-old lawyer was admitted to a Rochester hospital in August, 1954. He had been in apparent good health, apart from incompletely treated syphilis in his early twenties, until 8 days before admission. He then noticed mild bifrontal headache made worse by coughing and movement. Vomiting occurred 2 days later, followed after another 2 days by some loss of vision in the left eye. The next day his left eyelid began to droop. Two days before coming to the Mayo Clinic, he became confused for a few hours and was taken to a local hospital, where lumbar puncture was done; "80 to 90 red cells" were found in the cerebrospinal fluid. On admission to the hospital here, he complained of total blindness in the left eye and "spotty" blindness in the right, general malaise and frontal headache that was increased by coughing and movement. He had noted decrease in the sense of smell for 1 year.

Examination disclosed a tall man with somewhat acromegaloid facial features but with normal hands and feet. He was drowsy but oriented and could answer questions and obey commands. Neurologic examination showed bilateral Babinski's sign, more prominent on the right. Kline, Kolmer, Hinton and Kahn serologic tests for syphilis all gave positive results.

On the day of admission, the left pupil was dilated and fixed; it was considered that some light perception was present in the left eye but that vision was much impaired on this side, with some impairment on the right. On the following day, the patient's near vision on the right was recorded as 14/42 with the aid of a +2.00 lens; vision on the left was restricted to counting fingers. The field of the right eye was contracted temporally, while that of the left was contracted temporally and below. Grade 3 paralysis of the left third nerve was noted, with possible paresis of the fourth nerve. Papilledema was absent. It was suggested by the ophthalmologist that the picture could be caused by bleeding into a pituitary adenoma.

Roentgenograms of the skull showed enlargement and decalcification of the sella turcica (Fig. 1*a*). Electroencephalography showed bilateral frontosylvian delta waves, maximal on the left side, and generalized grade 2 dysrhythmia suggestive of a lesion in the midline. The basal metabolic rate was −23 per cent.

The patient appeared to be holding his own temporarily but 2 days after admission it appeared that his condition was worsening. Ophthalmologic examination at this time showed temporal anopsia on the right, with a central scotoma, while the left eye was amaurotic (Fig. 1*b*). Complete paralysis of the left third nerve was present and the left pupil was fixed; the right pupil reacted to convergence but not to light.

To exclude an aneurysm of the circle of Willis, possibly of syphilitic origin, left carotid angiography was done with thorium dioxide (Thorotrast). This did not show any evidence of aneurysm but the carotid siphon was deformed as by a pituitary tumor. Left transfrontal craniotomy was done on the same day. The patient received cortisone by intramuscular injection as part of the preoperative preparation. Bloody fluid was encountered around the chiasm, and the optic nerves were bowed back by the dark capsule of a hemorrhagic pituitary adenoma. The left optic nerve was ecchymotic. The capsule was incised and a portion was resected. It contained sticky black blood typical of hemorrhagic infarction of a pituitary adenoma. This

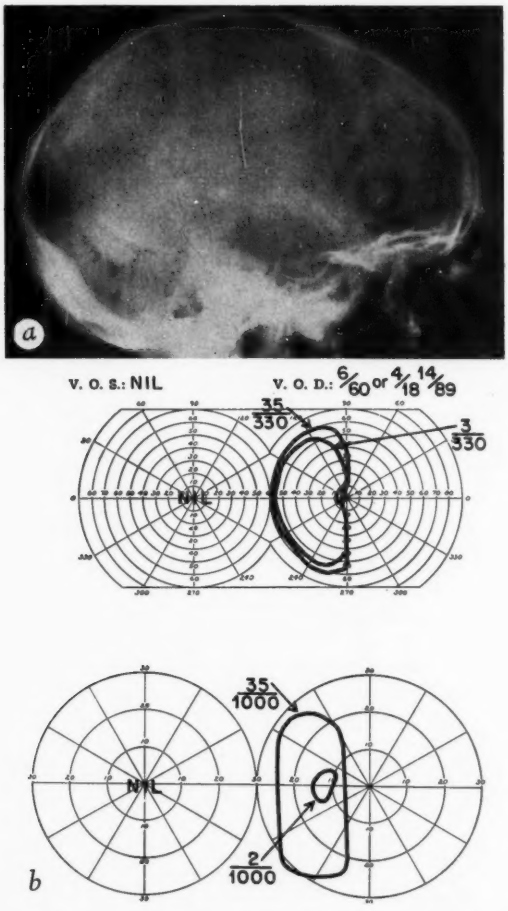

FIG. 1. *Case 1.* (*a*) Lateral roentgenogram indicating slight enlargement of sella turcica. (*b*) Preoperative visual fields on Aug. 20, 1954.

old blood and a good deal of adenomatous tissue were removed by section and curettage. The type of adenoma could not be identified histologically because of necrosis.

Mild expressive aphasia was present for 2 days after the operation but, apart from this and an episode of supraventricular tachycardia, the patient's convalescence was uneventful. Administration of cortisone was continued for several days after operation. Light perception returned quickly in the left eye, and the patient volunteered that he had return of vision in the left eye by the 2nd postoperative day, at which time the ptosis had lessened. Nine days after operation, ophthalmologic examination showed great improvement in central vision on the left, with filling in of most of the right temporal field and much of the nasal field of the left eye (Fig. 2*a*).

The fundi were essentially normal, with possible minimal pallor of the right disk. Residual paralysis of the left third nerve was present, with ptosis now graded as +2 to +3. Upward and outward rotations were graded as −1, with downward rotation graded −2; the left pupil was still irregular and fixed but the right was normal. The patient was dismissed on the same day.

Examination 4 months later showed grade 1 pallor of the left disk. The right disk was normal. The right visual field was almost normal and the left field was filling in slowly (Fig. 2*b*). Gross limitation of ocular movements was absent. Vision in the

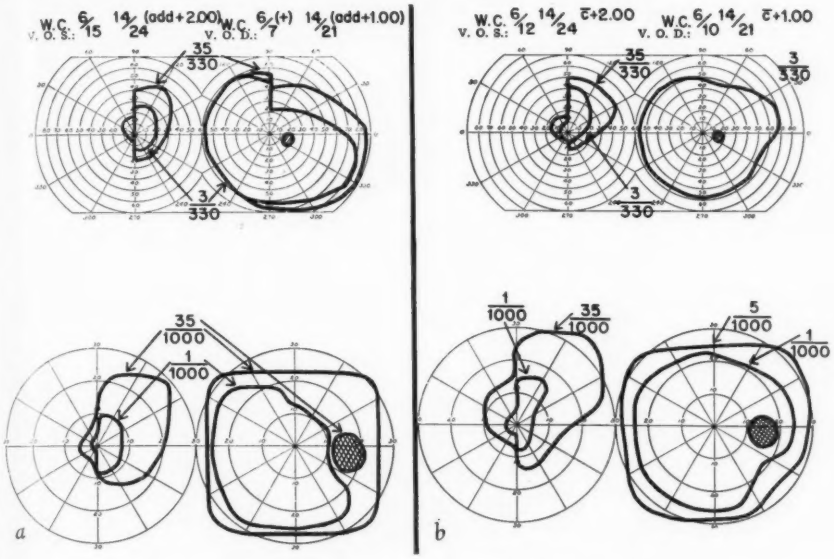

FIG. 2. *Case 1.* (*a*) Visual fields on Aug. 30, 1954, which was 9 days after operation. (*b*) Visual fields on Dec. 6, 1954.

left eye was 6/12 and that of the right was 6/10. The patient showed no signs of diabetes insipidus and his condition was satisfactory. He has since returned to the bench as a circuit judge.

Case 2. A 62-year-old man first came to the clinic in March, 1954, complaining of loss of vision. He stated that his beard had always been scanty. He had noted loss of libido about 6 years prior to admission here, and 3 years previously he had begun to have intolerance to cold. Nine months before he was seen here, he had had the "flu," after which he noted that his sight was almost gone.

Examination showed bitemporal hemianopsia, with a right central scotoma (Fig. 3*a*). The vision was 6/6 in the left eye but only 1/60 in the right; both optic disks showed some pallor, grade 1 on the left and grade 2 on the right. It was considered that these findings indicated a lesion of the chiasm and the right optic nerve. The patient was somewhat acromegaloid, with large hands and feet and prognathism. The basal metabolic rate was −8 per cent. Roentgenograms of the skull revealed pronounced enlargement and decalcification of the sella turcica by an intrasellar

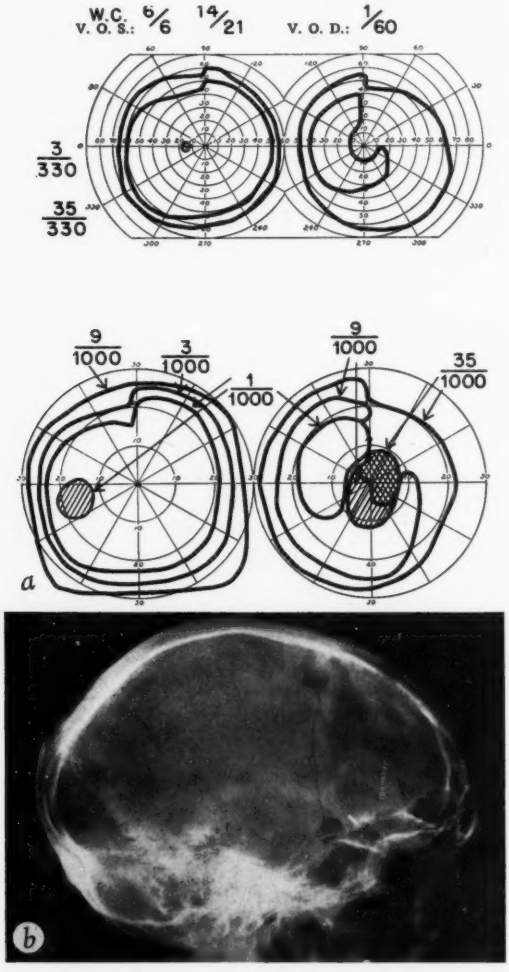

FIG. 3. *Case 2.* (*a*) Preoperative visual fields on Mar. 24, 1954. (*b*) Preoperative lateral roentgenogram showing great enlargement of the sella.

tumor (Fig. 3*b*). Since the patient had resolving pneumonitis at the base of the lower lobe of the right lung, it was decided to defer operation and to give roentgen therapy instead. This was done over a period of 16 days.

He returned to the clinic in August, 1954, complaining of further loss of vision. At the time of this admission, he was drowsy and did not co-operate well in visual-field testing. His fields had narrowed, with further loss in the left, or "good," eye, so that at this time he had left upper quadrantic homonymous anopsia (Fig. 4*a*). These findings were still thought to indicate a right chiasmal lesion. The pallor of

his disks was as before. The electroencephalogram showed bitemporal grade 2 delta waves and generalized grade 2 dysrhythmia, somewhat more pronounced on the left side. A waxing and waning effect was present, and the record was considered to indicate a midline lesion, possibly extending more to the left side. Since the patient's vision had failed progressively after roentgen therapy, surgical intervention was advised.

Right transfrontal craniotomy was done after the patient had received cortisone for several days. The arachnoid was yellowish and showed numerous adhesions. The

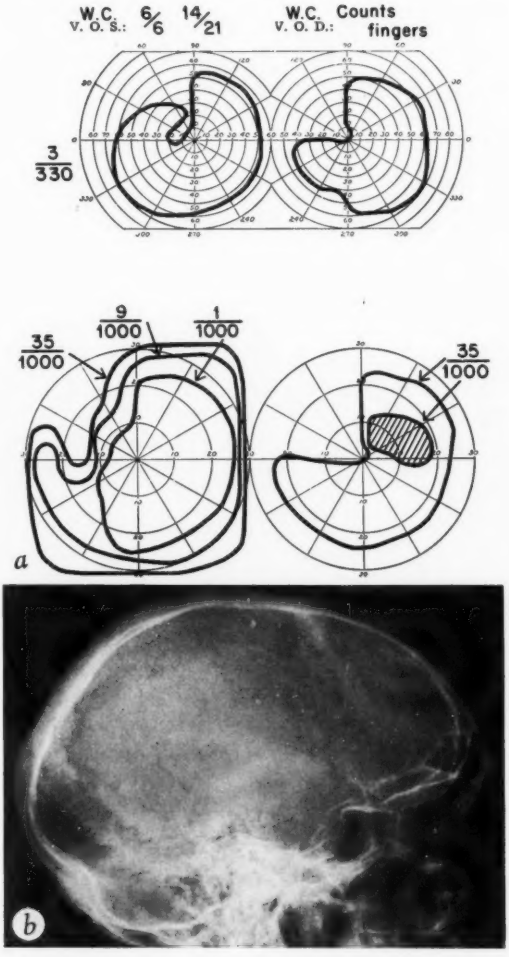

FIG. 4. *Case 2.* (*a*) Later preoperative visual fields on Aug. 4, 1954, showing further visual loss after roentgen therapy. (*b*) Postoperative lateral roentgenogram showing a fluid level under the bone flap.

cerebrospinal fluid was lemon-yellow. The pituitary gland was enlarged and contained several cystic adenomas, two of which extended outside the sella on either side. The gland itself was pressing against the third ventricle. The cysts contained old blood and degenerated pituitary adenoma of nonspecific type.

During the postoperative phase, the patient was at times drowsy, facetious or confused. His blood pressure was unstable but he had no fever. Since he was not improving as anticipated and because roentgenograms of the skull suggested a fluid

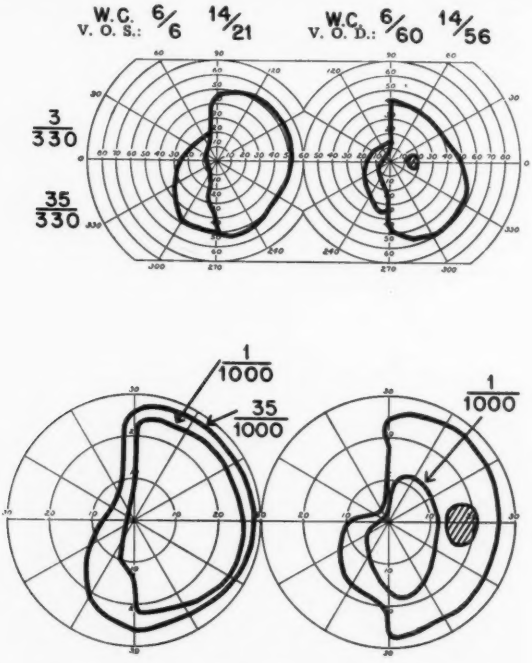

FIG. 5. *Case 2.* Visual fields 2 months after operation.

level under the bone flap (Fig. 4*b*), the wound was opened on the 11th postoperative day; a loculated extradural and subdural collection of bloody cerebrospinal fluid was found under the frontal lobe. This was evacuated and the patient's subsequent course was uneventful. Eighteen days after operation, the pallor of the left optic disk was graded 3 and that of the right was graded 1. It was thought that further loss of vision was present on the left but the patient's poor co-operation made it difficult to be certain of this. His pituitary function was considered to be at the preoperative level, with no evidence of diabetes insipidus.

Two months later, his visual fields were relatively unchanged (Fig. 5) but the pallor of the disks had receded to grade 2 on the left and grade 1 on the right, and the patient was in good health.

The patient was readmitted to the hospital in April, 1955, for myxedema, drowsi-

ness, mental confusion and disorientation. He promptly improved in 2 weeks on a regimen of hormonal substitution therapy. Some improvement was noted in his visual fields.

PATHOLOGIC ASPECTS

It appears to be agreed[7,16,23,27,34] that the essential cause of this complication of hemorrhage is that the tumor outgrows its blood supply; in other words, growth of the tumor leads to compression of blood vessels supplying the adenoma, which in turn gives rise to necrosis and hemorrhage. The pressure resulting from the hemorrhage also may compress adjacent vital structures. Histologically, various degrees of mixed necrosis and hemorrhage are seen,[7] and there may be no real purpose in distinguishing one from the other. Müller and Pia[27] pointed out that the walls of the blood vessels of the adenoma may be extremely thin or even calcified and thus are likely to bleed. In some reports,[4,27,40] trauma has been cited to explain the hemorrhage. For the present, there appears to be no obvious relationship between hemorrhage and the type of the tumor,[24] although Brougham's group[7] thought that necrosis and hemorrhage are most common in eosinophilic adenomas. Many of the patients who had hemorrhage in pituitary adenomas did have clinical evidence of acromegaly.[2,6,9,16,17]

COMMENT AND SUMMARY

The term "pituitary apoplexy" has been coined for the sudden catastrophe in which patients have acute hemorrhage into a pituitary adenoma. We consider that the 2 cases that we have reported are not true instances of "pituitary apoplexy" because several criteria were wanting. Our 2 cases illustrate the fact that the presence of acute hemorrhage into a pituitary tumor must be suspected in any patient who suddenly loses his vision, even though clinical signs of a pituitary tumor may not have made themselves grossly manifest. The early diagnosis of acute hemorrhage into a pituitary tumor is obviously imperative to save vision, to prevent pressure on adjacent vital structures and to relieve the inevitable increased intracranial pressure that may be incompatible with life. Hemorrhage into a pituitary tumor during roentgen therapy is one of the major complications of this therapy for these lesions. This complication must be recognized at all times. In other instances, as in our first case, the diagnosis must be suspected when acute loss of vision occurs. Lateral roentgenograms of the skull will give great aid in diagnosis, but the plotting of accurate visual fields in a patient whose condition will permit such studies usually gives the key to the solution.

Internal decompression of the hemorrhagic cyst generally suffices for treatment, as recurrent bleeding seldom takes place. Adequate opening of the cyst wall or total resection of the tumor and capsule precludes reaccumulation of fluid within the cavity. Subsequent roentgen therapy may be deemed advisable depending on the patient's general condition. Hormonal

replacement therapy, as in our second patient, usually will be required, since the acute hemorrhage plus surgical intervention frequently destroys any remnants of active pituitary glandular tissue. It is for this reason that roentgen therapy may be contraindicated.

The preoperative preparation of each patient by administration of cortisone appears indicated, as these patients tolerate the surgical procedure better if they are prepared adequately with hormones. Both our patients received cortisone both before and after operation. This is especially true if the patient already shows signs and symptoms of pituitary insufficiency. Such patients should receive cortisone and, in many instances, testosterone or thyroid or both.

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CONSIDERATIONS CONCERNING INCREASING CEREBRAL BLOOD FLOW IN CEREBRAL INSUFFICIENCY*

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EXPERIENCES in the past and more recent clinical and experimental information indicate that it seems possible to increase the blood flow to a cerebral hemisphere by means of repeated temporary carotid compression. Considerations concerning this observation are briefly summarized and illustrated in this paper.

I. *Past Experience.* Rudolph Matas[17] employed carotid compression by several mechanical means for inducing collateral flow to the ipsilateral hemisphere, prior to carotid ligation. He pointed out that Halsted[12] had first used such a compression method, the aim being "to obtain by gradual occlusions a secondary development of the collateral circulation in parts liable to suffer by insufficient vascular supply."

Halsted[12] applied an aluminum band to a common carotid artery, almost occluding it, and observed: "Even in this case slight head symptoms persisted for several months making it seem likely that complete occlusion would have been followed by severe symptoms if not by death." Halsted concluded that "The partial occlusion of arteries discloses a suggestive and, I believe, a promising field for investigation in physiology and experimental pathology."

Dandy[9] also found that patients could tolerate a gradual occlusion of a carotid artery but not an acute, complete interruption of flow. He stated, "regardless of age, the adequacy of the collateral circulation must be known before operation (carotid ligation). If inadequate, it can be made adequate by partially occluding the internal carotid, thus forcing the collateral branches to take up the increased burden and later permit its total ligation without hazard."

II. *Clinical-Pathologic Evidence.* A common clinical observation is the ability of patients to recover from cerebral vascular occlusions because of an improvement in the cerebral circulation. Neurologic defects often reverse in patients with occlusions in various parts of the circulation. A silver clip, for example, placed upon the anterior choroidal artery may result in a definite but temporary neurologic effect.

The neuropathologists have recognized that the infarcted area in a brain

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is of lesser area than that normally supplied by the involved artery. Also, the vessels within the infarcted area contain fluid blood indicating that collateral circulation has been present.

Our experience has also shown that patients with carotid occlusions (partial or complete) caused by atheromatous disease at the carotid bifurcation develop an increasing tolerance to contralateral digital carotid compression. Syncope with or without chronic convulsive movements usually occurs abruptly after 12 or 15 seconds of total occlusion of the contralateral vessel upon the first compression test. In some of these patients cardiac slowing with a fall in blood pressure occurs, unaffected by atropine. In others, the cardiac effect is minimal. These responses are quite different from the cardiac arrest resulting within several seconds after compression of the "hypersensitive carotid sinus." The response to digital compression in patients with occlusions gradually becomes less marked and requires a longer period of compression. Subsequently, in some cases, the syncopal effect cannot be induced. Finally, the symptoms of dizziness, blurred vision and faintness fail to appear. These responses seem to occur in the younger age groups, possibly related to the absence of advanced generalized arteriosclerosis.

The observation has also been made that following carotid ligation, early compression of the contralateral carotid produces syncope. A tolerance then develops because of increasing collateral blood flow.[8]

Kussmaul and Tenner[15] in 1859 reviewed in considerable detail the experiences of the past concerning temporary carotid occlusions. These authors described the use of carotid compression by Caleb Parry[18] in the treatment of hysteria and convulsions, the experiments of Jacobi[14] and many others. None had made mention of convulsions occurring, although such effects as "dimness of sight, dizziness, stupor, weakness in the legs, staggering, swooning, loss of consciousness and sudden apoplectic falling down" were observed. Kussmaul and Tenner emphasized that compression of both carotids also may result in "all the symptoms of a slight epileptic attack" as well as unconsciousness. Not all the experiments produced this effect since "collateral circulation is kept up by the vertebral arteries." It is of interest that after 100 years, these same observations are remade on the basis of one compressed carotid and one that is obstructed by disease.

Until the observations of Weiss and Baker,[21] who stressed the importance of the carotid sinus reflex mediated through the 9th nerve, the carotid artery claimed little attention in this century. Although these authors recognized a "cerebral" type of "reflex," the etiology was ascribed to a "cerebral vasoconstriction" produced by an ill-defined neural mechanism. Now after another 20 years, we must return to the older 19th century concepts which recognized the effects of cerebral ischemia produced mechanically.

III. *Angiographic Evidence.* Angiographic studies have confirmed earlier pathologic studies which showed that a collateral blood supply may be demonstrated following the occlusion of major vessels. A "cross-over" effect may occur in an occlusion of the carotid artery (Fig. 1). The middle cerebral

artery may restore flow to the tissue supplied by an anterior or posterior cerebral artery. The posterior cerebral arteries may supply blood to the anterior portion of the circle of Willis and to the basilar artery. The external carotid may enlarge, as may the ophthalmic branch of the internal carotid, and thus supply the middle cerebral artery. The flow of blood in the ophthalmic artery reverses (Fig. 2).

IV. *Experimental Evidence.* Cinemicrophotographic studies of the pial circulation in monkeys under Nembutal anesthesia have revealed a remark-

FIG. 1. Thrombosis of right internal carotid artery. Left carotid injection resulted in extensive visualization of the right side from the left.

able ability of the pial arteries to dilate (but not to constrict). Arteries varying in size from 20 to 150 microns can expand to twice and three times their calibre under varying conditions (passage of emboli, segmental obstruction, administration of CO_2, loss of blood, elevation of blood pressure). Reversals of blood flow may be observed. Arterial shunts have been photographed. Large oil emboli, 25 to 30 microns in size, pass through capillaries measuring 10 microns (Figs. 3, 4, and 5).

Laboratory evidence in monkeys suggests that the pial circulation has the ability to provide anastomotic flow.

V. *Anatomical Studies.* Experimental work in the past devoted to studying the vascular pattern of the brain has employed the injection of various

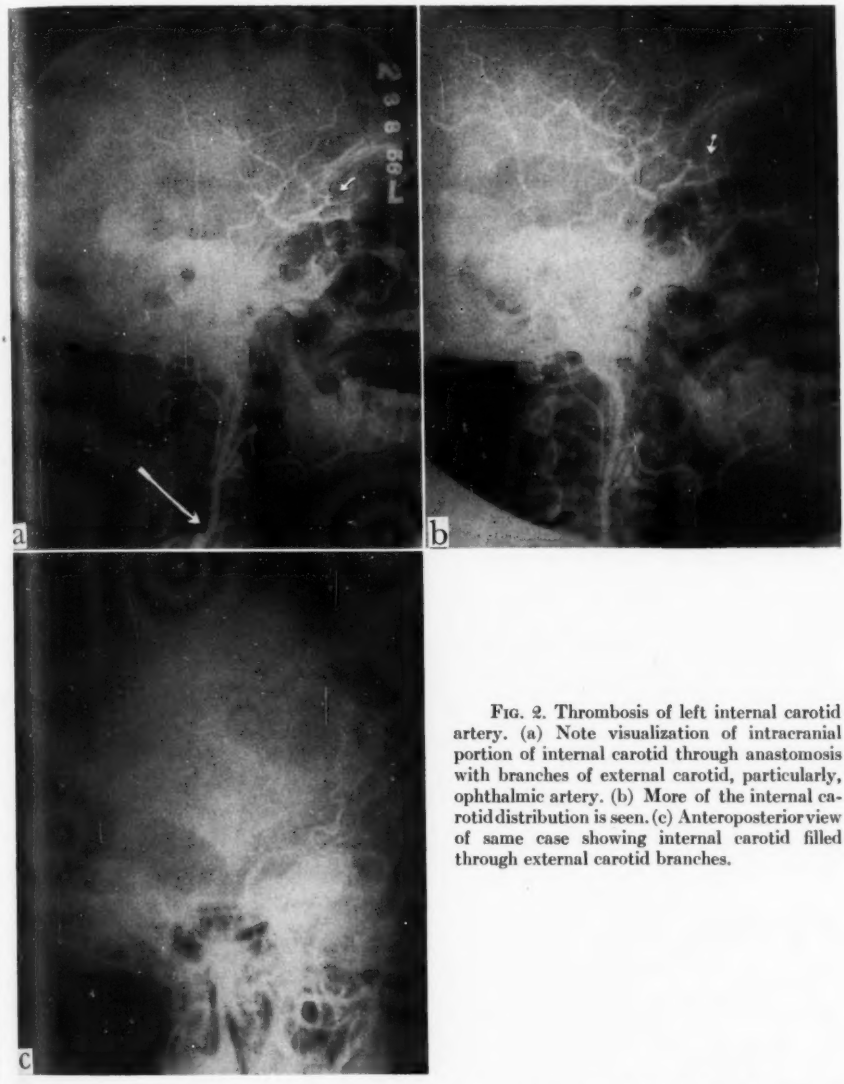

FIG. 2. Thrombosis of left internal carotid artery. (a) Note visualization of intracranial portion of internal carotid through anastomosis with branches of external carotid, particularly, ophthalmic artery. (b) More of the internal carotid distribution is seen. (c) Anteroposterior view of same case showing internal carotid filled through external carotid branches.

materials into the vessels in postmortem specimens (Cohnheim,[7] Duret,[10] Heubner,[13] Beevor,[4] Shellshear,[20] Abbie[1] and others[3]).

The individual conclusions reached varied somewhat because of the differences in technics used (type of medium injected, pressure of injection, method of analysis of the preparations) and also the differences in terminology used to describe results.

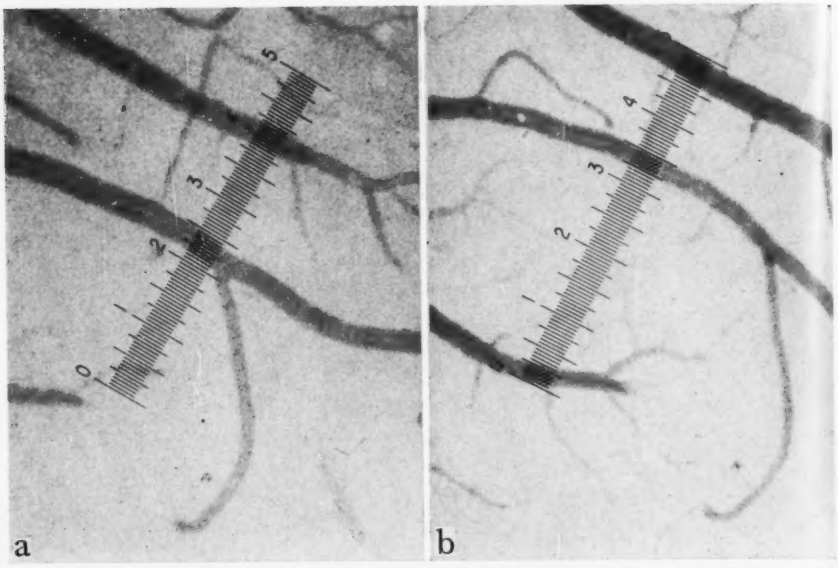

FIG. 3. Collapse of pial vessels in the monkey under anesthesia following reduction in blood volume resulting in hypotension. (a) Normal tension and (b) hypotension.

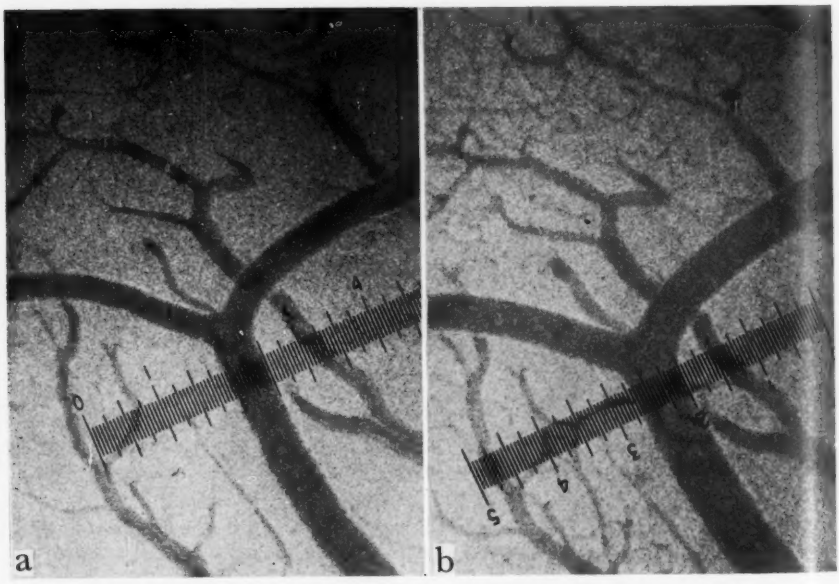

FIG. 4. Dilatation of pial vessels in the monkey under anesthesia following inhalation of CO_2. (a) Before and (b) after inhalation.

Clinicians, such as Charcot and his followers, developed clinical concepts based upon the experimental evidence that best explained observable neurologic patterns. An area of infarction of the cerebral tissue supplied by the "lenticulostriate artery" was attributed to an occlusion of that vessel since such arteries did not have collateral communications. Limited experimental data in dead brains combined with faulty clinical premises developed a concept of "end arteries" which underestimated the capillary, supracapillary and arteriolar circulation. Then too, attention was focused upon the branches of the arterial tree rather than the trunk (the carotid). The cerebral circula-

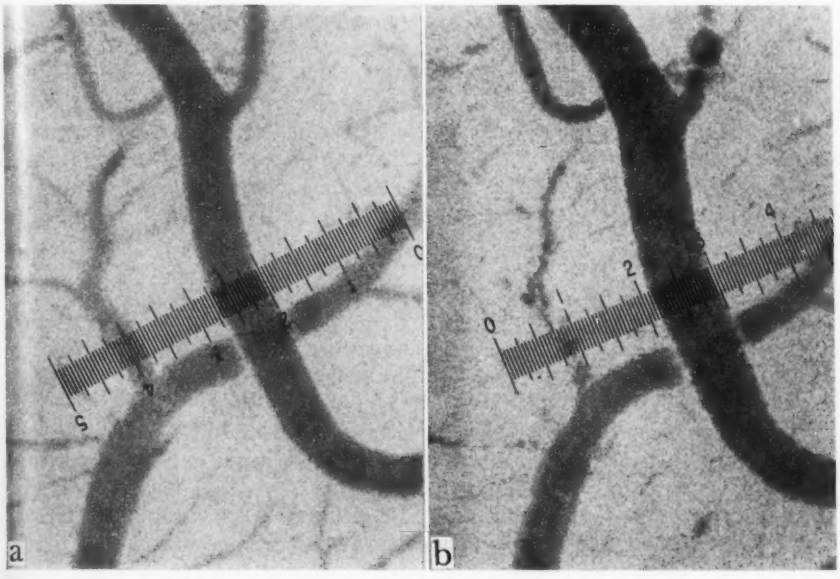

FIG. 5. Mechanical enlargement of pial vessels in the monkey under anesthesia when the vessel is obstructed by an embolus. (a) Before and (b) after embolism.

tion was viewed as a static system by the clinician as well as by the pathologist. The dead injected brain with red and blue rubberized vessels dominated clinical thinking.

Later experimental evidence has been important in initiating the newer thinking. This work has come from Lorente de Nó,[16] Pfeiffer,[19] Adams,[2] Cobb,[6] Fay,[11] Campbell[5] and many others.

CONCLUSION

Recently, newer clinical views pertaining to cerebral vascular disease have been gaining recognition. The study of the dynamics of cerebral blood flow provided by angiography and a renewed interest in the subject by pathologists and clinicians have modified the older ideas.

Infarction is influenced by the sufficiency of blood flow in the network of vessels surrounding the area nourished directly by the occluded vessel or vessels. The clinical pattern of symptoms and signs is related to this crucial relationship and can be interpreted on the basis of reversible or irreversible cellular damage. Such a phenomenon as "spasm" or "constriction," which cannot be identified as occurring in vessels of such calibre, is not needed as a clinical concept. Sympathetic blocks may have an effect upon the cerebral circulation when the external carotid artery is the important source of collateral flow.

A reasonable conclusion, based upon theoretical evidence and confirmed by our limited experience, is that patients who have experienced a reduction in blood flow by occlusions involving the carotid bulb, the siphon, and the major branches of the circle, may be benefited by daily, temporary, digital, contralateral carotid artery compression to encourage anastomotic blood flow. Such compression can be employed cautiously and for short intervals at first, gradually increasing the period as the patient's responses improve. Patients with complete unilateral carotid occlusion may benefit by this procedure to prepare for future occlusion of the good carotid.

SUMMARY

1. The effect of occlusive vascular disease involving the brain depends upon collateral circulation.

2. The collateral circulation can be demonstrated by angiography.

3. The ability of pial vessels to dilate significantly suggests that flow can be increased.

4. Compression studies of the carotid indicate that the cerebral circulation can become accustomed to a reduction in flow from one carotid, either complete or partial.

5. Compression of the carotid may be of value in encouraging collateral flow in the treatment of a cerebral vascular insufficiency syndrome.

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OBSERVATIONS ON UNILATERAL COMPRESSION AND PALPATION OF THE CAROTID BIFURCATION*

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WHEN a ligation of the common or the internal carotid artery is desirable, evaluation of the competency of the cerebral circulation before the ligation is extremely important. Compression of the carotid arteries for testing the adequacy of the circulation gives valuable information. Conditioning of the cerebral circulation by repeated compressions of the carotid, as suggested by Matas,[7] Dandy[1] and others, is possible and it is a valuable means of obtaining better results.

During the past 50 years there have been varying opinions concerning the results of unilateral palpation and/or compression of the carotid bifurcation. Before the days of "the irritable carotid sinus," syncopal effects from compression of the carotid bifurcation were thought to be caused by ischemia of the brain. Since the outstanding work of Hering,[5] Heymans[6] and others on the carotid sinus as one of the governing mechanisms of the blood flow to the brain, there has been a tendency to consider all abnormalities resulting from palpation and/or compression of the carotid bifurcation, the consequences of "irritable carotid sinus." Manipulations of the bifurcation have been described as a means for relief of anginal pain by Freedberg and Riseman.[2] Others ascribed the production of anginal pain to such palpation or compression.[3,9] Hypersensitivity of the carotid sinus may be present with hypertensive disease and arteriosclerosis, according to Weiss and his coworkers.[11]

With a view to clarify the confused state of our present-day knowledge concerning this subject it was thought advisable to record our experiences with palpation and compression of the carotid bifurcation in patients with unilateral occlusion of the internal carotid artery and in cases in which a carotid ligation was carried out for certain intracranial aneurysms, arteriovenous malformations and arteriovenous fistulae.

Unilateral palpation and/or compression of the carotid bifurcation may result in several different effects. In normal patients there may be no abnormality noted. In others, a syncopal effect may be produced. Syncope as a result of such manipulations may be caused by (1) an irritable carotid sinus, (2) an ischemia of the brain produced by the compressive occlusion of the internal carotid artery and (3) a combination of irritable carotid sinus and ischemic effects, or a combination of (1) and (2).

(1) The importance of the carotid sinus as a governing mechanism of

* Aided by the Kresge Foundation.

blood flow to the brain was first appreciated by Hering[5] and later analyzed more critically by Heymans[6] and his co-workers. Experimentally, a lowering of the intrasinus pressure by compression of the common carotid artery, proximal to the sinus, results in cardiac acceleration, vasoconstriction and a rise in arterial pressure with liberation of adrenalin. Pressure against the carotid bifurcation causes a slowing of the heart rate, vasodilatation and a fall in blood pressure. In men, increased irritability of the carotid sinus region may result in pathological states which are: (1) a bradycardia and asystole with eventual syncope, (2) a precipitous drop in blood pressure associated with syncope but without bradycardia, (3) a stimulation of brain centers causing unconsciousness and syncope through glossopharyngeal-vagal influences unassociated with bradycardia or fall in blood pressure (the cerebral type), and (4) a combination of the above types. It is difficult to say whether the so-called "cerebral type" is a valid form of the effect of irritable carotid sinus. The presence of bradycardia and asystole and a drop in blood pressure can be easily recorded, but an unconscious state resulting from stimulation of the brain-stem centers from an irritable carotid sinus is more difficult to prove, particularly if the compression were severe enough to produce an ischemic effect, which may also cause an unconscious state.

(2) When the carotid arteries are compressed sufficiently to cause an occlusion of the internal carotid artery an ischemic effect may result, characterized by syncope in about 15–25 seconds of compression. If the opposite carotid artery is adequate, if the basilar circulation is adequate, compression of the internal carotid artery on a given side may not cause any abnormality in the absence of an irritable carotid sinus. If, on the other hand, there is a partial occlusion of the internal carotid artery on the opposite side, if there is a thrombosis of the internal carotid artery on the opposite side, if there is a generalized atheromatosis of the brain so that compression of the carotid on either side causes an inadequate amount of the blood flow to the circle of Willis, a cerebrovascular insufficiency with syncope may occur.[4,10] In the presence of inadequate posterior and anterior communicating arteries in the circle of Willis, cerebrovascular insufficiency may occur when the carotid arteries in the neck are compressed on the side of the small or absent communicating vessels. We have been particularly impressed by the ischemic type of syncope in the past 5 years because of the amazing frequency of internal carotid artery thrombosis in the neck. In most of these patients compression-occlusion of the patent carotid artery causes syncope. The same is also true in most patients who have had one carotid artery, either internal or common, ligated for a cerebrovascular abnormality. Compression of the normal carotid artery for 15–25 seconds in such a case frequently results in syncope soon after the ligation. In some patients tested 6 months to 2 years after the ligation there has developed sufficient conditioning of the cerebral circulation so that compression of the patent carotid artery does not cause a completely unconscious state but does result in many instances in dizziness, extreme nervousness and a feeling of faintness.

(3) A combination of "irritable carotid sinus" with cerebrovascular insufficiency on carotid compression is a common finding, particularly among patients with cerebrovascular disease. In many patients with thrombosis of the internal carotid artery in the neck, palpation and compression of the carotid on either side may result in evidence of an "irritable carotid sinus" (Figs. 1 and 2). Atropinization in such a patient may counteract the irritable carotid sinus and yet the patient may have syncope as a result of the ischemic effect of the occlusive compression of the vessels of the more normal side. That there is an increasing irritability of the carotid sinus region in patients with coronary disease, and possibly also with cerebrovascular diseases, is a conclusion deserving credence since many of our patients belong in the cerebrovascular and cardiovascular disease category.

MATERIAL

The material is based on compression studies of over 40 patients and will be discussed under the headings of (1) changes in the pulse rate, (2) changes in the blood pressure, (3) changes in the state of consciousness, (4) changes in the electroencephalogram and (5) angiographic changes.

Changes in the Pulse Rate. Changes in the pulse rate are quite common on palpation and compression in the neighborhood of the carotid bifurcation. A drop in the pulse rate may occur without any appreciable abnormality in the conscious state or without any other symptoms such as dizziness or headaches. In some cases mild palpation of the carotid bifurcation resulted in the bradycardia without any changes in the conscious state. In the same patients compressive occlusion of the vessel resulted in syncope if the opposite carotid artery were defective (thrombosis of the internal carotid artery or partial occlusion of the bifurcation). In many instances it was noted that atropinization resulted in partial improvement of the bradycardia. That is, following atropinization the patient's pulse was increased about 25 per cent and compression or palpation of the carotid bifurcation resulted in some drop in the pulse rate but not as much as without atropine. In some patients in whom compressive occlusion of external and internal carotid arteries resulted in unconsciousness, mild palpation of the bifurcation resulted in bradycardia. In other cases bradycardia was extremely severe with long periods of asystole. Examples are shown in Figs. 1 to 4. In those patients with severe asystole, syncope developed in 8–10 seconds. In some cases bradycardia occurred almost immediately after the beginning of the palpation of the carotid bifurcation and in many instances there was a vagal escape, with an increase in the pulse rate in the period of the palpation of the vessel.

Changes in the Blood Pressure. A precipitous drop in blood pressure seldom occurred in our cases. Most of our patients were studied in a sitting-up position; a few were also studied in a lying-down position. Vagal effect with marked bradycardia and asystole with syncope or cerebrovascular insufficiency on compressive occlusion of the internal and external carotid arteries

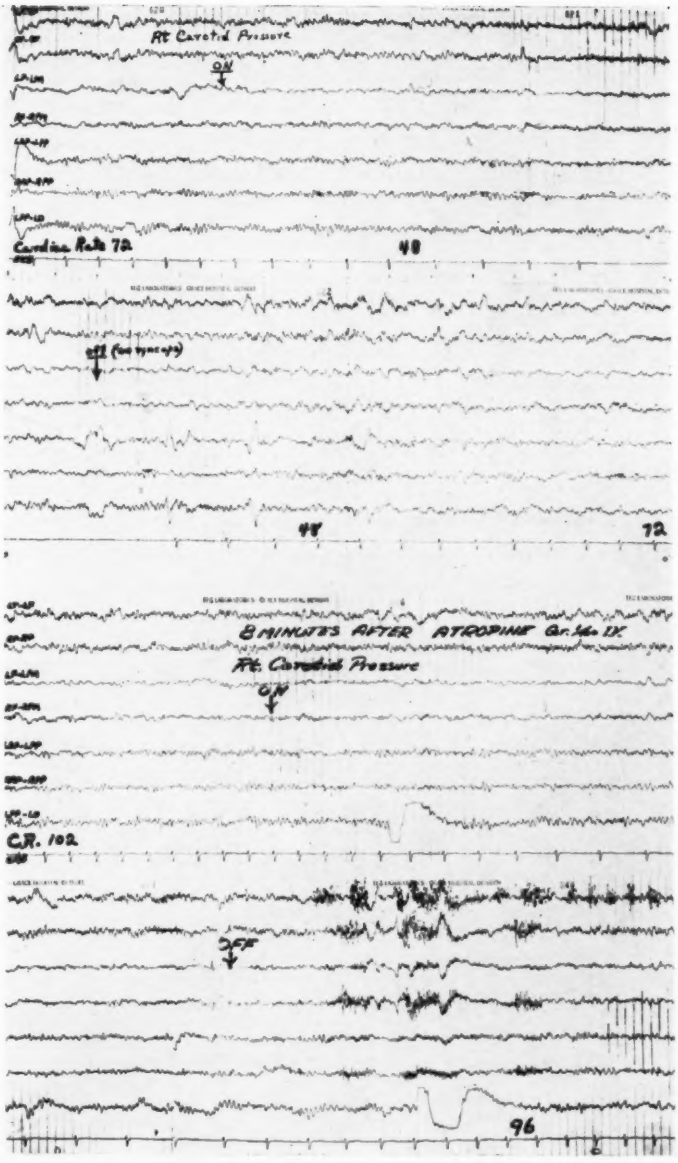

FIG. 1. Carotid bifurcation compression tests in a patient 64 years of age, with thrombosed right middle cerebral artery. Mild manipulation of carotid bifurcation resulted in a drop in pulse rate from 72 to 48, with asystole lasting about 6 sec. After the manipulation was stopped the pulse rate reached 72 in 19 sec. Following the injection of 1/100 gr. of atropine intravenously, the pulse rate was 102 in 8 minutes and another manipulation of the right carotid bifurcation resulted in a drop in the cardiac rate (68) but not as severe as the pre-atropine drop. The pulse rate increased to 96 in 5 sec. Severe compression of the left carotid area resulted in a syncope in this patient. Mild manipulation resulted in changes in the pulse rate unassociated with syncope.

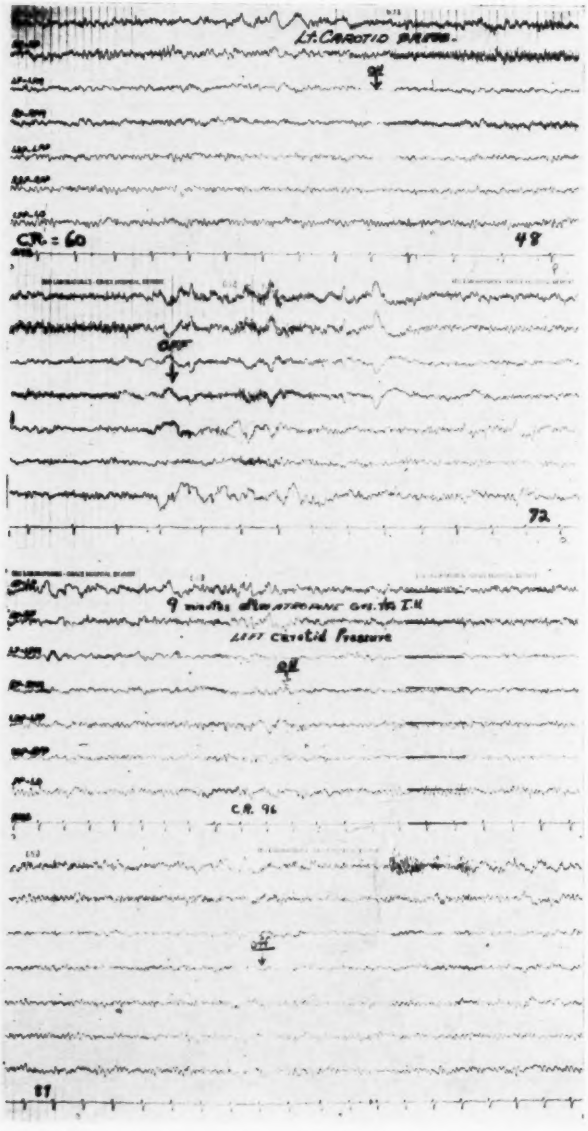

FIG. 2. Left carotid bifurcation compression and manipulation in the patient in FIG. 1 resulted in a small drop in the pulse rate but the effects were much less when atropine was injected. Occlusive compression of the left carotid bifurcation resulted in syncope in 20 sec.

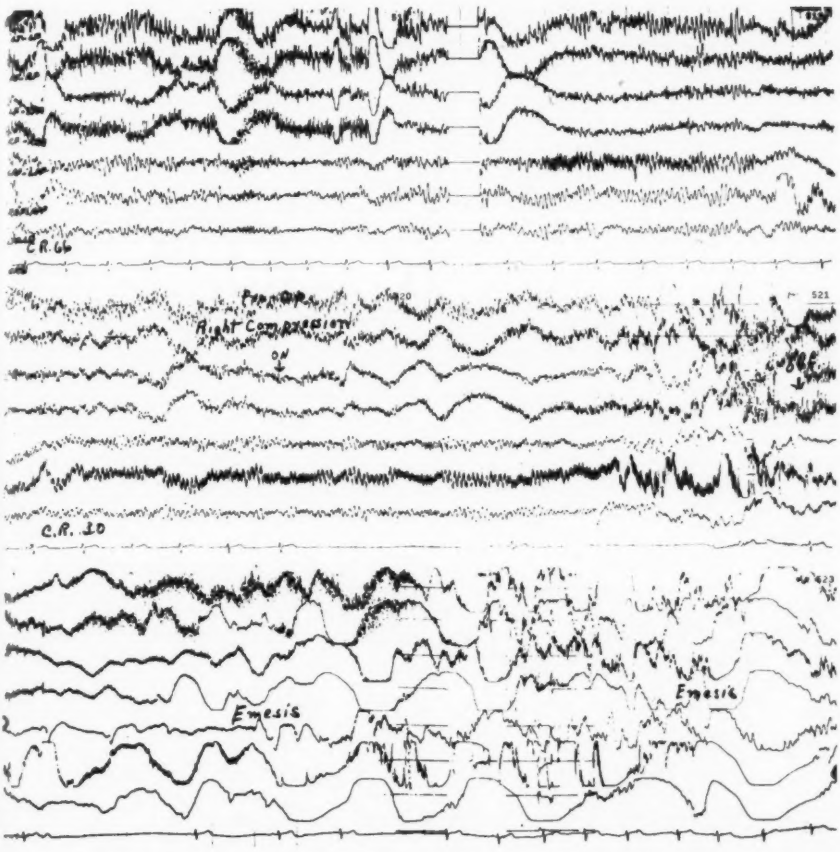

FIG. 3. A 46-year-old female, with an aneurysm of the right middle cerebral artery, was thought to be a candidate for right common carotid artery ligation. Palpation-compression revealed the presence of a severe irritable carotid sinus with asystole and syncope occurring in about 10 sec. This patient became unconscious on mild manipulation of the right side of the neck, not only around the bifurcation but lower down. Note the marked lowering of the heart rate following the beginning of the compression. Note that during a period of 20 sec. there were only three pulsations of the heart. During her syncopal attack she also had several vomiting spells suggesting a vagal stimulation. After complete atropinization and the use of local anesthesia and local infiltration with novocain hydrochloride, her right common carotid artery was ligated.

were the usual result. Mild falls in blood pressure were noted in several instances but these mild falls could not explain the syncopal effect. Small drop in blood pressure continued to occur even though the patient was atropinized (Fig. 5).

In operations upon the carotid bifurcation, manipulation of this area, particularly by traction, resulted in precipitous drop in blood pressure in at least 5 instances. These drops were of the order of 40–90 mm. of mercury.

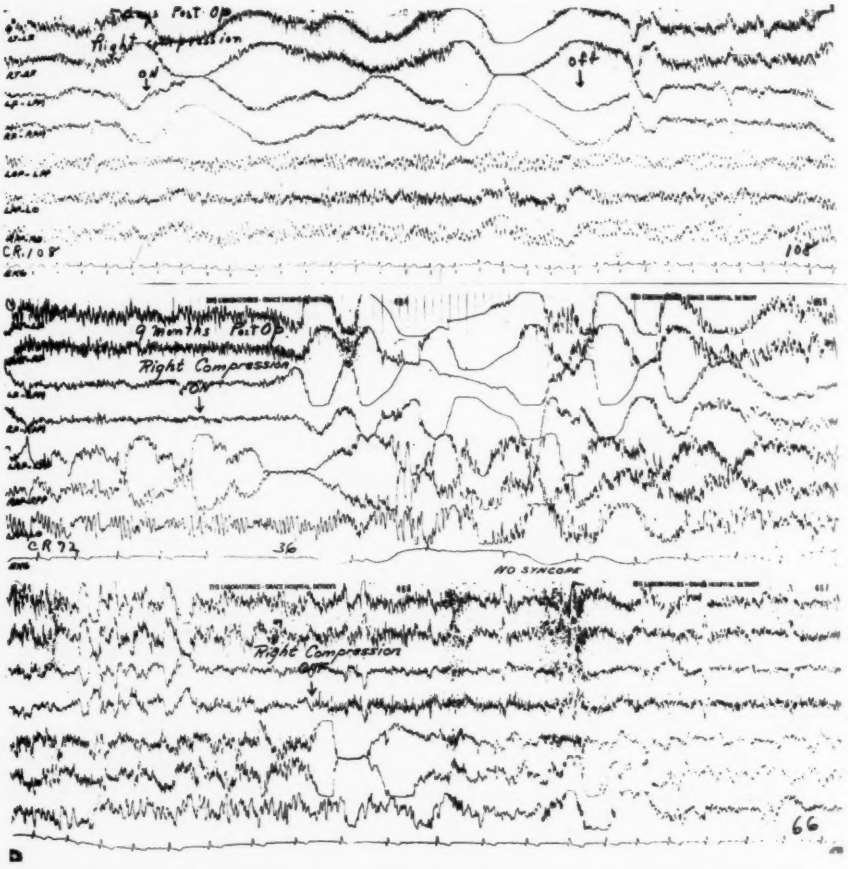

FIG. 4. Showing the record of compression in neighborhood of right carotid bifurcation 5 days after ligation of right carotid artery and denervation of the carotid sinus. The cardiac rate remained 108 throughout; no dizziness or syncope was caused by the manipulations. The lower portion of the record of the same patient 9 months postoperatively shows some return of the sinus effect with a drop in the cardiac rate from 72 to 36 on right carotid compression and manipulations. There is, however, a rapid escape even before the compression is stopped, with recovery of the pulse rate to about 66. The bradycardia in this case may be the result of regeneration of some of the sinus fibers.

This was in spite of the fact that most of these patients were prepared with atropine and the area of the operative traction was infiltrated with novocain hydrochloride solution.

Changes in the State of Consciousness. The syncopal effect was produced under 12 seconds in the cases in which an "irritable carotid sinus" was stimulated. In patients who had cerebrovascular insufficiency produced by compression of the internal carotid artery on a given side, unconsciousness

occurred in a period of 15–20 seconds or longer. The greatest majority of the patients studied belonged in the latter group. A syncopal effect from the "irritable carotid sinus" was seen less frequently. Whether or not the time of unconsciousness may differentiate the syncope of the carotid sinus abnormality from syncope caused by cerebrovascular insufficiency is still being studied critically and more information may be forthcoming as our experience increases. However, the material thus far suggests that this differ-

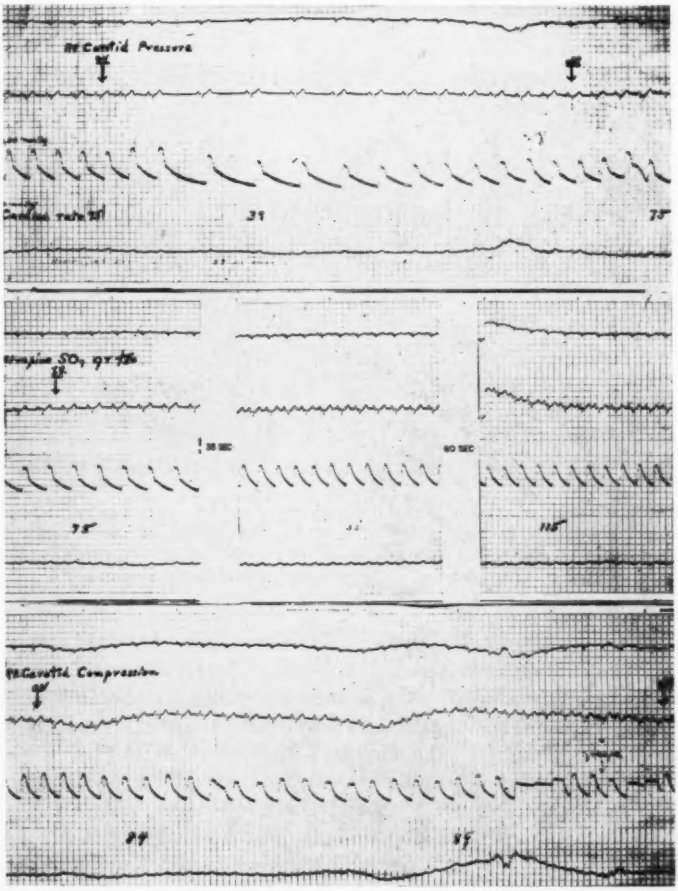

FIG. 5. Continuous blood-pressure record in a patient with thrombosis of the left internal carotid artery. Compression of the right carotid, shown in the upper row, resulted in bradycardia, a drop in blood pressure and syncope at the end of 15 sec. The cardiac rate dropped from 75 to 39. Intravenous injection of 1/150 gr. of atropine increased the pulse rate from 75 to 115 in 60 sec. Occlusion-compression of the right carotid 3 min. after the injection of atropine resulted in a syncope at the end of 18 sec. but with no associated bradycardia. The patient's pulse rate had stabilized at 84 per min. The blood pressure dropped 35 mm. during the compression.

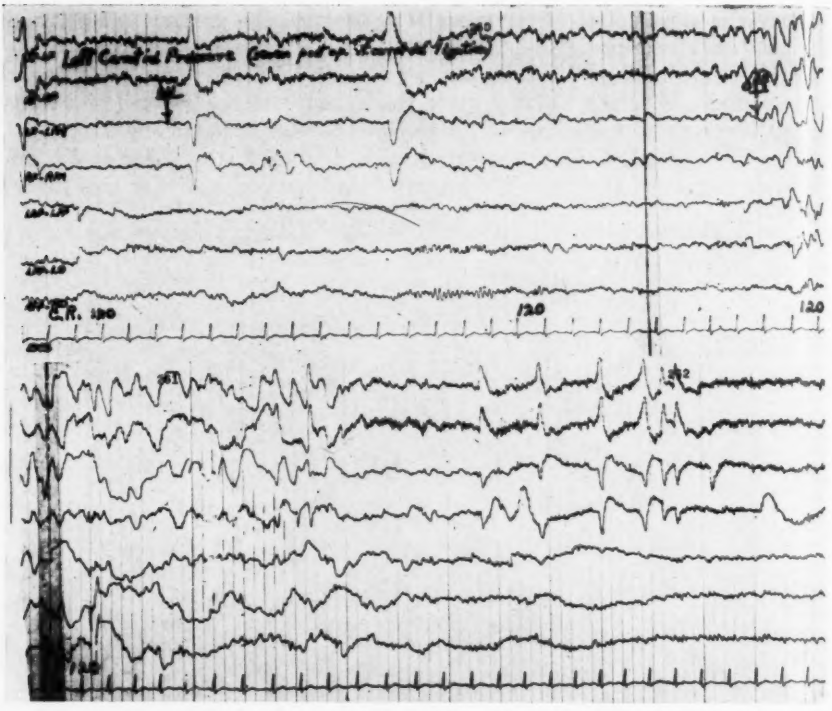

FIG. 6. A 26-year-old patient was treated by ligation of the right common carotid artery for an arteriovenous malformation of the right parietal area. Compression of the left carotid artery bifurcation resulted in a syncopal effect at the end of about 13 sec. with severe changes in the electroencephalogram bilaterally. The electrocardiographic record shows a cardiac rate of 120 throughout.

entiation may be valid. It should be kept in mind that in the process of looking for the pulsating vessels in the neck there may be some stimulation of the carotid sinus with bradycardia before compressive occlusion is carried out. The investigator should keep this important point in mind and give the signal for the beginning of the compressive occlusion at the proper time.

Changes in the Electroencephalogram. Changes in the electroencephalogram were characterized by a slowing of the record, particularly in the frontal and parietal leads (Fig. 6). This was somewhat more marked on the side of the compressed internal carotid artery. Testing patients for possible cerebrovascular inadequacy by electroencephalographic control was not dependable, as other authors have emphasized. We are in agreement with other authors that electroencephalographic abnormalities may occur in patients who can tolerate a carotid ligation, and comparatively normal records following compression do not rule out the possibility of complications after ligation. The value of the electroencephalogram in the

diagnosis of thrombosis of the internal carotid artery in the neck is also questionable.

Meyer *et al.*[8] suggested that in the presence of internal carotid or basilar artery insufficiency a fall in blood pressure from tilt-table manipulations may result in focal abnormalities in the electroencephalogram. They found that positional hypotension was greater among patients with cerebrovascular insufficiency when treated with a tilt-table. Whether or not further experience will parallel the electroencephalographic abnormalities or lack of abnormalities observed in patients for carotid ligation should be seen in future contributions.

Angiographic Changes. Angiographic studies are extremely valuable in evaluating cervical compression tests. A partial or complete occlusion of the internal carotid artery may be demonstrated in some patients who become unconscious on compression of the carotid bifurcation on the normal side. The presence of an occluded basilar, anterior or middle cerebral artery may be contributory to the vascular insufficiency when compression tests are carried out. Angiography of both carotids and the vertebral should be obtained in all such cases.

Important Considerations in Compression-Palpation Tests of Carotid Bifurcation. In doing palpation and compression tests the following appear to be valuable: (1) For the purpose of noting the presence of an irritable carotid sinus, complete occlusion of the vessel by compression is not needed. When the vessels are so compressed as to occlude them the possibility that there may be an ischemic effect has to be kept in mind. Weiss and Baker[11] emphasized that in the older individual compression had to be rather severe in order to obtain an effect. It is our impression that in a certain number of this group there may have been vascular insufficiency caused by occlusive disease on the opposite side, in the basilar distribution or at the base of the brain. (2) Atropine is a valuable testing agent since vagal effects may be counteracted by its use. Although in some instances bradycardia disappears completely after atropinization, in others the bradycardia may be less marked than if atropine were not used. (3) When abnormalities occur as a result of compression tests, the possibility that there is occlusive disease of the opposite side has to be considered. In patients who have a thrombosed internal carotid artery, compression of the internal carotid artery on the patent side may result in syncope. This is not proposed as a test for this condition but when it is seen, the possibility of a thrombosis of the internal carotid artery on the opposite side should be considered. This is particularly true when adequate atropinization has counteracted the vagal effects. (4) It is important when doing compression tests to record the pulse rate by using one of the electroencephalographic channels for electrocardiographic recording. In this manner valuable information is obtained. Its use has made it possible to analyze a great many cases in which there was a combination of an irritable carotid sinus of varying degrees and cerebrovascular insufficiency when the carotid was compressed. A continuing record of the

blood pressure also would be valuable in connection with some of the cases of irritable carotid sinus.

SUMMARY AND CONCLUSIONS

(1) Unilateral palpation and/or compression of the carotid arteries in the neck may give invaluable information concerning the adequacy of the cerebral circulation as well as the presence of an irritable carotid sinus. Such palpation and/or compression tests may result in a syncopal effect (i) from an irritable carotid sinus, (ii) from cerebrovascular insufficiency when the compression stops the flow of blood to the head after 15–25 seconds or longer, and (iii) from a combination of (i) and (ii).

(2) An irritable carotid sinus may result in (i) a bradycardia with or without syncope, (ii) a precipitous drop in blood pressure with syncope but without bradycardia, (iii) reflex involvement of brain stem centers with syncope (?).

(3) In the cases so far studied it appears that cerebrovascular insufficiency with or without an irritable carotid sinus is the common cause for the syncope on unilateral compressive occlusion of the carotid arteries in the neck.

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VENTRICULO-AURICULOSTOMY. A TECHNIQUE FOR SHUNTING CEREBROSPINAL FLUID INTO THE RIGHT AURICLE*

PRELIMINARY REPORT

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THE treatment of hydrocephalus by establishing a communication between the cerebrospinal fluid pathways and the vascular system has interested surgeons since it was first suggested by Gärtner[5] at the National Science Convention in Lübeck in 1895. Despite the failures in the past, the idea remains alive and is being continually explored.

Eight years ago, with the help of engineers skilled in flow dynamics, we devised a ventriculo-venous shunt tube which included an encapsulated sleeve valve in its midportion. It was hoped that this valve would maintain a unidirectional flow of cerebrospinal fluid, prevent reflux of blood into the lateral ventricle and sustain the intraventricular pressure at or above the pressure at which the valve opened. In September 1953, we began a series of animal experiments designed to test this valve, and in April 1955 it was subjected to its first clinical trial. Because of the encouraging result in this first patient, we are presenting our data in the form of a preliminary report.

HISTORICAL BACKGROUND

In 1895 Gärtner[5] suggested that the most physiological method for treating hydrocephalus would involve establishing a connection with either the venous or lymphatic systems of the head and neck. During the two decades that followed, procedures incorporating these surgical principles were carried out by surgeons on the European and American continents.

Payr,[15] who published his experiences in 1908, was the first to attempt ventriculo-venous anastomosis. This author's first report concerns 3 patients in whom the lateral ventricle was connected to the longitudinal sinus using a segment of saphenous or temporal vein. All patients died within 4 months, but it was noted at autopsy that blood had not refluxed into the lateral ventricle and that the longitudinal sinus was not thrombosed.

In a later communication Payr[16] described further attempts to connect the lateral ventricle to the internal jugular vein. He used a formalin-fixed,

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paraffin-treated anterior or posterior tibial artery obtained from dogs or calves. A fresh segment of saphenous vein was drawn over the artery in a manner permitting an intima-to-intima junction with the internal jugular vein. The method was used in 8 patients, with 3 excellent results. In the 5 remaining patients his results were variable. The shunt was demonstrated to be patent at autopsy in some of his cases.

In 1911 Enderlen[4] connected a hydrocephalic ventricle with an enlarged superficial temporal vein by means of a freshly extirpated temporal artery. The anastomosis functioned "for a short period of time" and then blocked, following which the signs and symptoms of hydrocephalus returned.

Review of the American literature of the same period discloses that Kanavel[11] had thrust a vein "running upon the side of the head of the child" through a hole in the dural flap. It is not mentioned whether the vein entered either the subarachnoid space or the lateral ventricle. The result was unsuccessful. Beck[2] attempted a similar procedure in 2 patients without success.

In 1909 McClure[13] reported his attempts to connect the cisterna magna with the external jugular vein of 6 dogs by interposing an autogenous segment of femoral vein or contralateral external jugular vein. The animals were killed at periods varying from 3 weeks to 3 months. On the basis of gross observation, all tubes were non-functioning. It was concluded that if the flow of cerebrospinal fluid had been more copious the outcome might have been successful. The technique was tried in a 10-month-old infant, using a cephalic vein removed from the child's father. Unfortunately the infant died several hours after surgery of a "central thermic disturbance."

In 1913 Haynes[7] published the first of a series of papers characterized by a progressive loss of enthusiasm for establishing a cerebrospinal fluid shunt into the venous system. In his first paper, this author described 2 unsuccessful attempts to connect the cisterna magna of hydrocephalic infants with the venous system. In the first case the cisterna magna was connected to the occipital sinus in the region of the torcular with a rubber tube. In the second patient the cistern was anastomosed to a parietal emissary vein. Both attempts were unsuccessful. By 1915[8] he had operated on 12 patients. In his final paper in 1916, Haynes[9] remarked, "I claim that cisternasinus drainage is founded on logical and physiological conceptions. . . . " He reported that 5 of the 12 patients operated on had died in the immediate postoperative period. In the 7 survivors results were not encouraging and he stated, "I confess I am not very enthusiastic about curing these subjects."

In the Cameron Prize Lectures of 1925, Cushing[3] mentioned that he had attempted to connect the dilated third ventricle with the longitudinal sinus by passing a specially devised tube through the corpus callosum. While the result was inconclusive, he commented that blood did not pass from the sinus into the ventricle which suggested that pressure in the ventricle was always higher.

With the advent of plastics in surgery, it seemed that some of the technical difficulties associated with the establishment of a shunt might be lessened. In 1948 Ingraham *et al.*[10] attempted to divert cerebrospinal fluid from the enlarged ventricles of hydrocephalic dogs into the sagittal sinus, using a polyethylene tube. Direct observation of the shunt at surgery revealed that the system functioned well, but re-exploration 6 to 42 days later disclosed that in every case the blood had refluxed into the tube and clotted. These authors attributed the occlusion to the unfavorable differential in pressures between the ventricle and the sagittal sinus, presumably initiated by extremes in pressure during barking, straining and other conditions that raised intrathoracic pressure.

In the same paper the authors presented a second study in which cerebrospinal fluid was shunted from the lateral ventricle into the superior vena cava by means of a polyethylene tube. Again, after a short period of time clotting occurred and the system failed to function. Further attempts to utilize the valves of the facial, external maxillary and external jugular veins in conjunction with a polyethylene tube from the ventricles were likewise unsuccessful. These authors concluded, "Unless an extremely sensitive but completely competent artificial valve can be devised and introduced between the cerebrospinal fluid pathways and the venous system in such a fashion as to permit only unidirectional flow of fluid, no matter what the relative hydrostatic pressure may be, all attempts to achieve ventricular decompression by ventriculo-venous shunts will fail and should not be submitted to clinical trial."

In May 1949 Nulsen and Spitz devised a system utilizing two ball valves connected by a rubber "subcutaneous pump." This shunt was used to connect the lateral ventricle with the internal jugular vein in a 14-month-old infant with hydrocephalus. At the time of their report in 1951[14] the shunt had been functioning satisfactorily for $2\frac{1}{2}$ years.

In 1950 Gupta[6] reported his attempts to connect the lateral ventricle with the external jugular vein in 4 hydrocephalic infants. His results were inconclusive.

CASE REPORT

M.B., white female, was born on Jan. 4, 1955. She is the first-born child of young parents. Pregnancy was uneventful except for a "mild virus infection" in the first and third trimesters. The first stage of labor was of 7 hours' duration. The second stage lasted 54 minutes, and delivery was aided by the use of mid-forceps. When examined by one of us (A.H.H.) on the day of birth, the baby seemed normal in every way except for marked bilateral craniotabes and enlargement of the posterior fontanelle. The diameter of the latter was 4 cm. The circumference of the head was 34 cm.

Examination 5 days later disclosed that the circumference of the head had increased to 38 cm. and early hydrocephalus was suspected. Roentgenograms of the skull made at this time showed no abnormalities except for suggestive widening of the sutures.

By the end of the first month of life the circumference of the head had increased to 41.5 cm., and neurosurgical consultation was advised.

Examination. When examined on the neurosurgical service on Feb. 3, 1955, the abnormal enlargement of the head was apparent. Measurements were as follows: maximum circumference 42.5 cm.; ear-to-ear over vertex 24.5 cm.; chest at nipple line 34 cm. Veins of the scalp were prominent against a dusky cutaneous background. The anterior fontanelle was tense and did not pulsate even when the infant was held in an erect position. Auscultation of the head failed to disclose a bruit. Immediate hospitalization for further investigation and treatment was advised.

1st Hospitalization, Huntington Memorial Hospital, Feb. 7–Feb. 23, 1955.

Laboratory Findings. Hemogram was within normal limits for age. Urinalysis was negative except for a one-plus acetone reaction. Roentgenograms of the skull confirmed the abnormal enlargement accompanied by separation of the sutures.

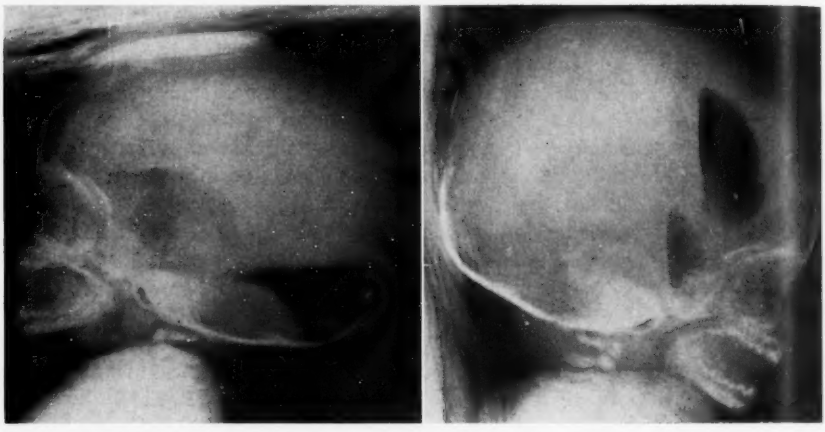

FIG. 1. Ventriculogram showing (*left*) marked enlargement of ventricular system rostral to aqueduct of Sylvius, and (*right*) marked enlargement of anterior portion of the ventricle.

Procedures. On Feb. 9, 1955 the right and left subdural spaces were tapped through the anterior fontanelle. Fluid was not encountered in either space. Accordingly, the needle on the left side was withdrawn, following which the needle on the right was advanced into the anterior horn of the lateral ventricle. Clear, colorless cerebrospinal fluid under considerable pressure gushed from the needle. One cc. of neutral phenolsulfonphthalein was injected into the lateral ventricle. A lumbar puncture was done and cerebrospinal fluid was allowed to drip freely into a glass beaker containing several drops of N/10 sodium hydroxide. At the end of 30 minutes the dye had not appeared in the lumbar subarachnoid space. A tentative diagnosis of obstructive hydrocephalus was made. This diagnosis was confirmed by a ventriculogram done later the same day which disclosed evidence of obstruction in the aqueduct of Sylvius (Fig. 1).

1st Operation. On Feb. 10, 1955, ventriculocisternostomy was performed under Sodium Pentothal-nitrous oxide-oxygen anesthesia, using an endotracheal tube, with the patient in the face-down position. A small suboccipital craniectomy was done and the dura mater was opened. The arachnoid was extremely thin and friable

and could not be satisfactorily sutured to the dura mater. After splitting the inferior portion of the vermis, the fourth ventricle and caudal end of the aqueduct of Sylvius were visualized. The ventricle was not dilated. Cerebrospinal fluid was not flowing through the aqueduct. An attempt was made to pass a soft rubber 8F catheter through the aqueduct. This maneuver resulted in an immediate respiratory arrest so the catheter was promptly withdrawn. After approximately 1 minute of artificial respiration, the baby began to breathe spontaneously. We then proceeded to join the posterior horn of the right lateral ventricle with the cisterna magna, using a

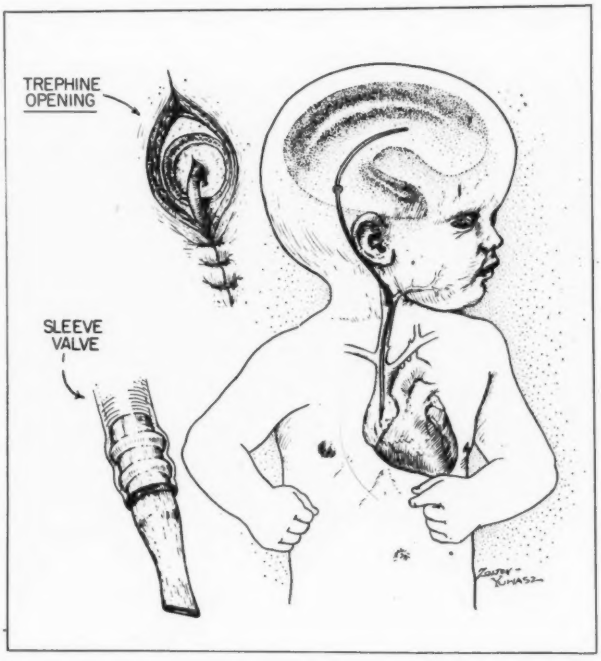

FIG. 2. Drawing of connection between cerebral ventricle and right auricle. The valve is located at the cardiac end of the shunt.

polyvinyl chloride tube 3 mm. in diameter. The wound was closed in layers with 4-0 black silk and the baby was returned to her room in good condition.

Postoperative Course. During the 2 weeks she remained in the hospital after surgery there was a considerable daily variation in tension of the fontanelle. At the time of her discharge from the hospital, the maximum circumference of the head was 45 cm.

2nd Admission. On April 4, 1955, approximately 2 months after the first operation, the infant was readmitted because of the failure of the ventriculocisternostomy to control her intracranial pressure. The circumference of the head had increased to 48 cm. At this juncture we decided to shunt the cerebrospinal fluid into the right auricle.

2nd Operation. On April 8, 1955, ventriculo-auriculostomy (Fig. 2) was done under ether-oxygen anesthesia. A Leigh valve was used for intubation. Preliminary roentgenogram of the chest was taken for measurement. The baby was postured lying on her back with the trunk and lower extremities resting on a pad. By turning her face to the left, we obtained a satisfactory exposure of the right side of the head and the anterior region of the neck.

An incision was made along the anterior edge of the right sternomastoid muscle and deepened to expose the internal jugular and common facial veins. These vessels

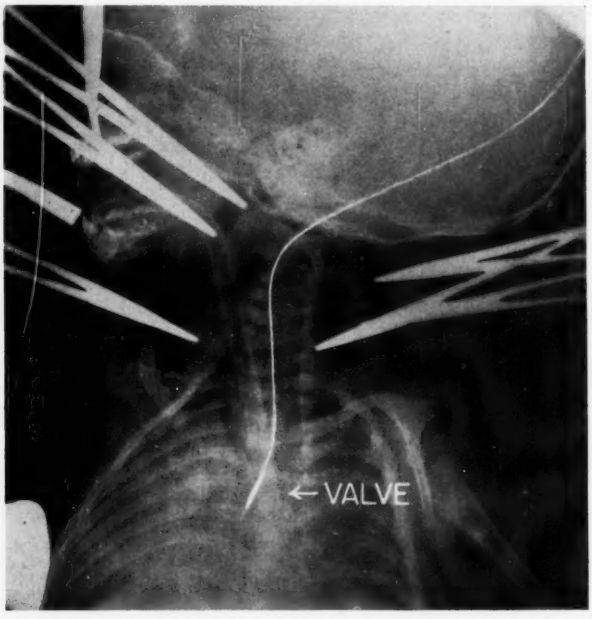

FIG. 3. Roentgenogram made during surgery after filling cardiac segment of shunt with 35 per cent Diodrast. The end of the tube is satisfactorily located in the right auricle.

were of equal caliber. Both veins were mobilized by passing silk ligatures under them and the wound was packed with moist gauze. At this point a 3 cm. incision was made in the right posterior temporal region. A burr hole 1 cm. in diameter was made and the dura mater was opened in a cruciate manner. A polyvinyl chloride tube, with an outside diameter of 2.08 mm. and an inner diameter of 1.57 mm., and with three holes cut in the side wall, was passed 7–8 cm. into the right lateral ventricle. Clear, colorless cerebrospinal fluid gushed from the other end. With blunt dissection a tunnel was made beneath the scalp just posterior to the mastoid process and the free end of the ventricular tube was brought into the wound of the neck together with the anterior margin of the sternomastoid muscle.

The cardiac segment also consisted of polyvinyl chloride tubing, having an outside diameter of 1.57 mm. and an inner diameter of 1.04 mm. A sleeve valve formed from tetrafluorethylene (Teflon) was fastened to the end of this tube. Preoperative testing showed that this valve opened when the pressure in the tube exceeded 3 cm.

of water. This tube was passed into the right auricle through the common facial and internal jugular veins. A roentgenogram made during the injection of 2 cc. of 35 per cent Diodrast through the tube confirmed the intra-auricular position of the valve (Fig. 3).

The two segments of the tube were joined by telescoping the smaller cardiac component into the lumen of the larger ventricular tube. Several 3-0 silk ties were placed around this joint. A 3-0 silk ligature was passed around the common facial vein to secure the tube within its lumen. The wound was closed in layers with interrupted sutures of 4-0 black silk.

Postoperative Course. During the first 2 weeks after surgery there was a disturb-

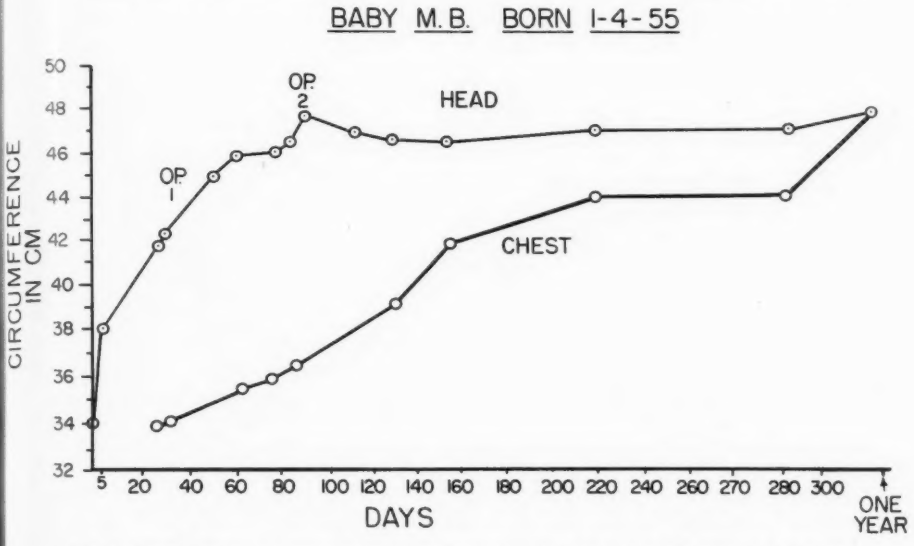

FIG. 4. Chart showing measurements of circumference of head and chest since surgery. Note that the head continued to enlarge after the ventriculocisternostomy but has not increased in size since the ventriculo-auriculostomy.

ing redness and swelling in the cervical wound but this gradually subsided and did not recur. The fontanelle remained depressed and at the time of discharge on April 30, 1955 the circumference of the head was 47 cm.

Since leaving the hospital the child has been reexamined at regular intervals. Enlargement of the head has been arrested (Fig. 4). When last examined on April 4, 1956, 1 year after the second operation, her mental and physical development was considered normal for her age. The anterior fontanelle was closed. The head and chest both measured 48 cm. in circumference.

COMMENT

A general revival of interest in methods for shunting cerebrospinal fluid into the circulatory system has led us to publish our experiences with this first patient. Subsequent to this original operation, we have collaborated with Anderson[1] in the clinical evaluation of this method and now have 23

cases under observation. Some minor changes have been made in the surgical technique. On the other hand, as a result of our studies in experimental animals, many improvements have been made in the design of the valve and in the tubing for the shunt. The original tetrafluorethylene sleeve valve has been replaced by a silicone slit-and-core valve molded into the tip of the cardiac segment of the tube (Fig. 5). Silicone rubber* is now being used exclusively for the shunt because of its more desirable physical and chemical properties, but we have continued to form the connectors from tetrafluorethylene.

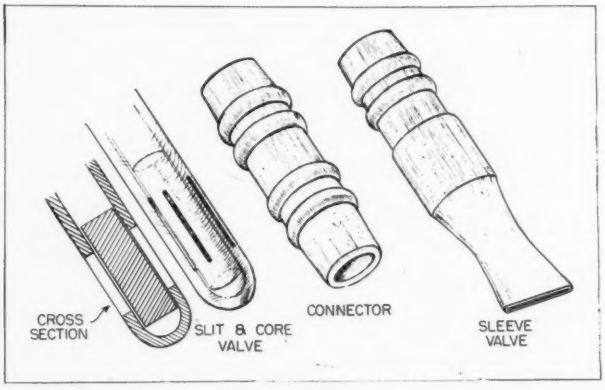

FIG. 5. Drawing showing the structure of the two types of valve used in the shunt. The tetrafluorethylene sleeve (Border) valve was used in the patient discussed herein. The silicone slit-and-core (Heyer) valve has been employed in our more recent procedures.

Successful use of this method requires that the valve at the end of the cardiac tube be properly located in the auricle so that it floats, as it were, in a pool of blood. Should the valve remain within the lumen of the internal jugular vein, it will be enveloped closely by the vessel wall and cease to function within a few days. We have proved this point to our satisfaction after testing many types of surgical tubing in the laboratory.

The chief advantages of this technique are (1) simplicity of the shunt, (2) minimal surgical trauma, (3) adaptability to even the smallest infant, and (4) retention of water, electrolytes and other cerebrospinal fluid constituents within the organism.

When disadvantages are considered, the chief deterrent to this procedure would seem to be the growth of the infant. This has not posed a problem thus far in our experience. To determine the rate of growth in the area spanned by the tube, we have collaborated with our pediatric colleagues in measuring the distance from the tip of the mastoid to the xiphoid in 64 children from birth to 5 years of age. In the newborn infant this measure-

* Dow-Corning S–2000 silicone tubing having an outside diameter of .083 inch and an inside diameter of .055 inch.

ment varies from 14 to 16 cm. and at 5 years from 20 to 22 cm., an average increase of 6 cm. This figure is considerably smaller than we anticipated. Furthermore, silicone tubing is elastic and easily lengthened by stretch. If the ventricular end of the tube is not fastened to the dura mater or surrounding tissues, it is possible that it will be slowly withdrawn from the ventricle with the growth of the head, neck and thorax.

Some will be concerned that the tube might slowly or suddenly migrate into the heart. While this possibility cannot be disregarded, we believe it to be unlikely if the tubing is properly secured to the tetrafluorethylene connector and the latter, in turn, is attached to the vein and surrounding tissue. As yet we have not observed propagating venous thrombosis or pulmonary embolism in either the clinical cases or experimental animals.

Finally, it is known that in many cases the hydrocephalus undergoes spontaneous arrest. In these patients, a ventriculo-auriculostomy would usher them through the most precarious period.

SUMMARY AND CONCLUSIONS

1. A technique for shunting cerebrospinal fluid from the lateral ventricle into the right auricle is described.

2. The successful use of this method in a female infant with obstructive hydrocephalus is presented.

The authors wish to acknowledge the invaluable assistance of Mr. R. L. Border, Jr., and Mr. W. T. Heyer in developing the intracardiac valves.

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ANEURYSMS ARISING AT THE INTERNAL CAROTID-POSTERIOR COMMUNICATING ARTERY JUNCTION*

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ONE of the commonest situations for intracranial aneurysms is at the origin of the posterior communicating artery from the internal carotid artery (Fig. 1). Theories have been put forward regarding the formation of a saccular aneurysm at this site.[13,17]

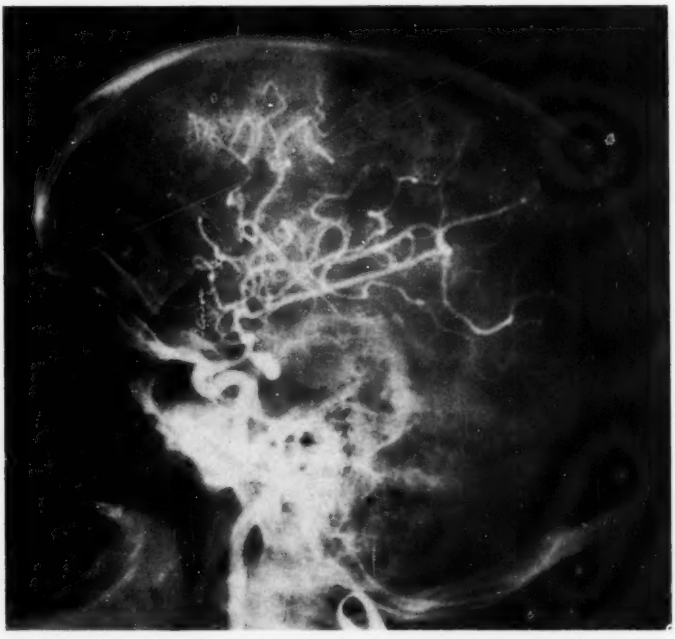

FIG. 1. Angiogram demonstrating aneurysm at junction of internal carotid and posterior communicating arteries, and also showing local arterial spasm.

Aneurysms of the posterior communicating artery are rare;[5,8,13,20] only one example has been seen in this Department.

Table 1 shows the location of the 326 intracranial aneurysms in our series. The aneurysms under discussion (90 cases) make up 27 per cent of the

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TABLE 1

Location of 326 intracranial aneurysms

Internal carotid artery	
Intracavernous	7
Carotid cavernous fistula	12
Ophthalmic artery	14
Anterior choroidal artery	4
Posterior communicating artery	90
Bifurcation	21
Unplaced	4
Total	152
Anterior cerebral artery and anterior communicating artery	87
Middle cerebral artery	73
Posterior cerebral artery	1
Basilar artery	9
Posterior inferior cerebellar artery	2
Vertebral artery	2
Total	174
Spontaneous subarachnoid haemorrhage	
Negative angiography	98
Angiography not performed	85
	183

total. An attempt will be made to study the angiographic appearances and clinical features of this group, and to evaluate the different methods of treatment.

Multiple aneurysms were found in 10 patients: bilateral internal carotid-posterior communicating artery in 2 (Fig. 2), anterior choroidal artery in 1, internal carotid artery bifurcation in 4, middle cerebral artery in 2, and ophthalmic artery in 1. Of the remaining 80 aneurysms, 39 were on the left and 41 on the right side.

Of the 90 patients, 66 were females, presenting with symptoms most commonly in the 5th decade; and there were 24 males, presenting most commonly in the 4th decade. Ages varied from 13–71 years.

CLINICAL FEATURES

The commonest symptom was subarachnoid haemorrhage, occurring in 75 patients, in 29 being the only symptom. In 34 it was recurrent, usually at about the 10th day. An associated oculomotor nerve palsy appeared in 29 patients, and a contralateral hemiparesis in 26; 2 of these had a temporal lobe haematoma, which was demonstrated by angiography. Cerebral anoxia occurring secondary to the sudden effusion of blood, and also possibly to arterial spasm,[14] was probably the cause of the hemiparesis in the others. Ten patients had subarachnoid haemorrhage, oculomotor palsy, and a contralateral hemiparesis.

FIG. 2. Angiogram showing anastomotic cross-circulation test. The contralateral internal carotid-posterior communicating artery aneurysm is also demonstrated.

Ipsilateral frontal and orbital pain are common initial symptoms and were found in 12 of our patients. Involvement of the basal structures and possibly pull on the internal carotid artery by the aneurysm cause this referred pain. It is an important symptom, indicating that treatment is urgently required,[6] and it is interesting that compression of the ipsilateral carotid artery usually abolishes it temporarily.

This type of pain is only occasionally associated with massive subarachnoid haemorrhage, but an ipsilateral oculomotor palsy appeared in 11 of these patients.

It is well known that this palsy is commonly found with aneurysms of the internal carotid-posterior communicating artery.[6,9] Forty patients in this series showed evidence of it, and in 4 it was the only feature. Five other patients had only dilatation of the pupil, suggesting a slight oculomotor nerve palsy. In 23 patients with subarachnoid haemorrhage, the palsy appeared on an average at the end of the 3rd week, but the time varied from 2 hours to 7 weeks. The paresis took about $2\frac{1}{2}$ days to become complete. In 14 patients with frontal pain the oculomotor palsy appeared about the 2nd week, taking about 6 days to become complete, but in 3 it came on with the frontal pain. In 4 there was an immediate palsy, associated with massive fatal subarachnoid haemorrhage.

The palsy can recover spontaneously, as was seen in 5 patients in whom it disappeared in an average of 4 months. Our experience in long follow-ups

regarding the prognosis of the oculomotor palsy has been similar to Jefferson's,[6] with incomplete recovery—especially of upward and downward eye movements, giving rise to a "regeneration syndrome" (10 of 40 cases), as shown in Fig. 3. Also, movements of the normal eye may cause reflex movements of the upper eyelid of the paretic eye.

The proximity of the aneurysm to the oculomotor nerve no doubt accounts for the paresis, but the trochlear, abducent and trigeminal nerves are close to the larger aneurysms, as is the optic tract. However, only a trochlear nerve palsy was seen occasionally in the patients in this series (5 cases).

An intracranial bruit was a very rare finding, being discovered in only 1 patient and disappearing immediately after ligation of the common carotid artery.

An attempt was made to correlate the size, shape and direction of each aneurysm with the clinical syndrome produced; but there did not appear to be any significant relationships.

ANGIOGRAPHY

Angiography is necessary for the diagnosis and anatomy of the aneurysm, to outline any other aneurysms, and to demonstrate the adequacy of the anastomotic circulation.

Very careful timing is required in ill patients before angiography can be carried out. Our practice is to do the investigation as soon as possible after the onset of symptoms, so that a decision may be made regarding treatment. Prolonged unconsciousness, severe confusion, or severe abnormalities of blood pressure will delay angiography. In addition, some patients were referred to this Department days or weeks after the onset of their illness, and therefore angiography was performed at a late stage in these patients. However, 26 patients had angiography within 7 days of the onset of their illness, and another 12 within 14 days.

We have found that fewer complications arise if general intratracheal anaesthesia is used, and also stereo roentgenograms may be taken more easily. Before the procedure the patient is given 200 mg. of papaverine intramuscularly, and the

FIG. 3. Photographs of patient. (*Upper two*) Immediately after rupture of aneurysm at left internal carotid-posterior communicating artery junction, showing an ipsilateral oculomotor nerve palsy; (*lower two*) 2½ years later, showing partial recovery of the palsy.

carotid sheath is infiltrated with a local anaesthetic.

There was a great variety in the size of the aneurysms, from $1\frac{1}{2} \times 1\frac{1}{2}$ mm. to 29×15 mm., and in their shape: globular, elongated, boot-shaped, and many were multilobular, and some had an irregular shape and density—suggesting partial thrombosis. But almost without exception, they were directed backwards, downwards and laterally. The average thickness of the "neck" was 2.7 mm., but it varied from 1.0 to 7 mm., and in 60 per cent was greater than 2.7 mm.

The anastomotic circulation between the two internal carotid artery systems is very important in relation to surgical treatment, and is routinely tested (Fig. 2). Eleven patients so tested had a poor or absent anastomotic circulation. In 3 of these patients a hemiparesis developed following ligation of the common carotid artery; but in 12 patients who had a good anastomotic circulation there also developed a hemiparesis. Thus there are other factors involved.

Especially after the treatment of intracranial aneurysms by carotid artery ligation, follow-up angiograms are important (see later). After ligation of the common carotid artery, percutaneous angiography is sometimes possible, but we prefer to examine the carotid vessels directly. Quite often they are mainly thrombosed; usually they are attenuated (Fig. 4). The operation and angiography are carried out under local anaesthesia.

There is a definite risk with angiography in patients who have had a subarachnoid haemorrhage recently. Arterial spasm[3] (Fig. 1) was shown in 11 patients, each of whom had bled less than 2 weeks previously. It was not seen in those who had not bled. When no aneurysm has been visualised in the angiogram of a patient who has had spontaneous subarachnoid haemorrhage, local spasm of one of the cerebral arteries has quite often given us a clue to the site of an aneurysm. Circulatory changes, in particular hypotension, may occur during angiography, and only a limited number of roentgenograms should then be taken.[2] One patient showed this to a marked degree, the blood pressure being unrecordable; unfortunately a similar response, which was fatal, occurred with clamping of the carotid artery. Autopsy showed marked anoxia of the ipsilateral cerebral hemisphere. A patient treated 9 years ago responded poorly to the test of anastomotic circulation, carried out 5 days after a severe haemorrhage. Severe circulatory changes appeared, he remained unconscious, a hemiparesis developed, and he died after 2 days. Autopsy showed extensive infarction in the distribution of the middle cerebral artery.

TREATMENT

It is emphasized that the timing and the type of treatment depend on the features of each individual case. Treatment is instituted as soon as possible following angiography, and is sometimes begun under the same anaesthetic as is used for the angiography. Thus surgical treatment was applied within 14 days of the initial symptoms in 31 patients. Thirty-two

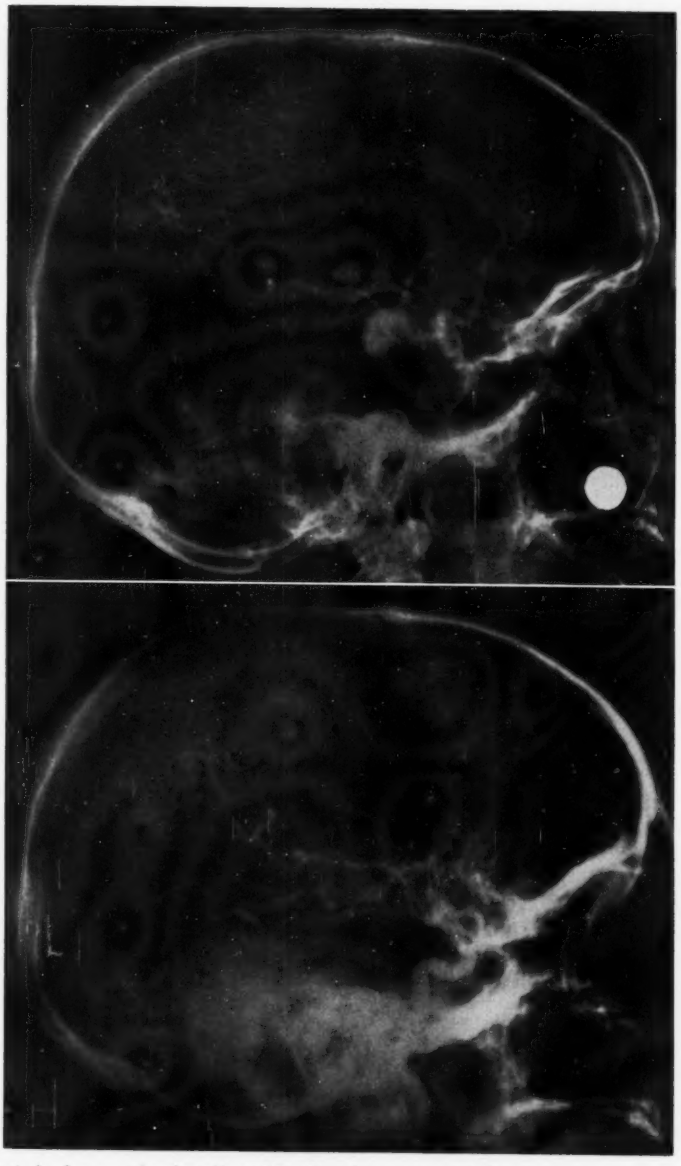

FIG. 4. Angiograms showing effect of ligation of common carotid artery on a large internal carotid-posterior communicating artery aneurysm after 6 weeks.

patients were treated prior to 1950, when our criteria for the management of these cases were somewhat different from what they are to-day.

Eight of the 84 patients whose symptoms were shown to be caused by an internal carotid-posterior communicating aneurysm were considered to be unsuitable for surgical treatment; 5 were critically ill on admission and 4 died; an inadequate anastomotic circulation was demonstrated in 2 patients aged 60 and 65 years, and 1 patient had a very small aneurysm which was unrecognized at the time. We agree theoretically with Uihlein and Hughes[19] that patients who are in a critical state following haemorrhage from an intracranial aneurysm may survive if they are treated immediately by hypothermia.

Two methods of treatment have been used mainly: 66 patients had a proximal ligation of carotid arteries in the neck, and 12 had an operation for direct obliteration of the aneurysm. The former method is preferred, but if there is no anastomotic circulation or only a poor one, if the aneurysm should fill during the test of contralateral anastomotic circulation, or if trial occlusion of the vessel results in neurological changes, a direct operation is indicated.

Our aim with carotid artery ligation is not only to diminish the propulsive force of the systolic pressure on the aneurysm[4,16,18] but also to alter the direction of the blood flow, so that the aneurysm is in a backwater. The common carotid artery is ligated first, and the internal carotid is ligated, usually after a period of about 3 months, only if follow-up angiography shows that the aneursym has not disappeared or become very much smaller. The vessel can be occluded over a period of days with a clamp,[7] especially in ill patients and in older patients, or it can be ligated immediately. But it is always tested by applying a clamp initially for about half an hour; and during the past year, on the suggestion of Professor Dott, a more critical test has been used. During the trial occlusion of the artery the patient's systolic blood pressure is dropped about 50 points with Arfonad given intravenously. If there are no neurological complications, the wall of the artery is stripped, producing a peri-arterial sympathectomy, and the vessel is ligated in continuity. Follow-up angiography (at 3 months) showed that the aneurysm had disappeared entirely in 7 patients, in 8 it was very much smaller, and in the remainder it was only slightly smaller (Fig. 4).

Much has been written about the complications that may occur after ligation of the carotid artery.[1,10–12,15] In this series (Table 2), a contralateral hemiparesis developed in 17 patients, on an average 17 hours after ligation. The patient's age was not important regarding the development of this complication, but patients over 50 years of age had only limited recovery subsequently. It may also be seen that in 3 patients this complication developed after direct obliteration of the aneurysm.

Arterial hypotension[12] was a feature in several patients after carotid artery occlusion, usually with severe neurological deterioration. Prompt treatment is required; immediate downward tilt of the patient's head, vasopressors such as methylamphetamine or Noradrenalin, and stellate

TABLE 2

Methods of treatment used, and their complications

Procedure	No.	Complications						
		None	Died	Recurrent Bleeding	Hemiparesis	Oculomotor Palsy	Psychological Changes	Epilepsy
Common carotid artery ligation	20	9	2	1	8	—	1	—
Internal carotid artery ligation	22*	13	2	—	5	—	1	2
Common and internal carotid artery ligation	22	13	2	(?1)	3	—	3	2
Common and external carotid artery ligation	1	0	1	—	—	—	—	—
Subtemporal decompression; evacuation of clot; common carotid artery ligation	1	0	—	—	1	—	—	—
Proximal ligation of carotid arteries in the neck	66	35	7	1	17†	—	5§	4
Direct obliteration of aneurysm	12	6	—	1	3‡	3	3‖	3
Total	78	41	7	2	20	3	8	7
Evacuation of haematoma	3	2	1	1	—	—	—	—

* One case: ligation of internal carotid artery below and above the aneurysm.
† Of brief duration with full recovery in 12; more severe in 4; 7 associated with hypotension.
‡ All severe; 1 associated with hypotension.
§ Brief duration and mild in 3; delayed in 1; severe in 1.
‖ Mild in 1; severe in 2.

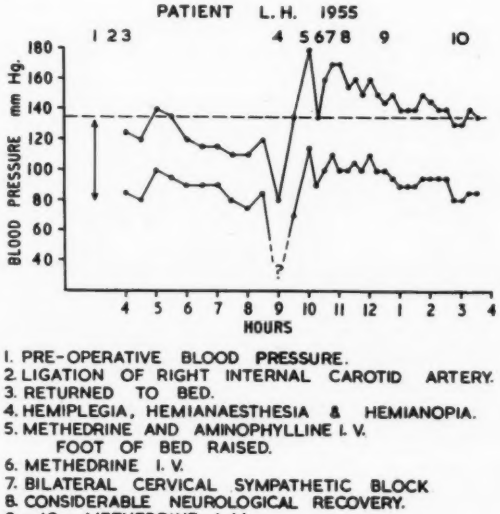

FIG. 5. Chart showing hypotension subsequent to ligation of internal carotid artery and result of treatment.

ganglion block may help (Fig. 5). After 2–3 days the blood pressure usually becomes stable. The nursing staff must be carefully tutored regarding this complication. Hypotension is not the only factor. Schorstein[15] and Brackett[1] stress the importance of the general and of the cerebral circulation in relation to carotid artery ligation; arterial spasm may be important. Although thrombosis occurs, it has often not extended as far as the common carotid bifurcation 3 months after ligation—even in patients who had a post-ligation hemiparesis. Most observers feel that embolism is an unlikely cause.[1,9,15]

In 5 patients after proximal ligation of the carotid artery there were psychological changes (Table 2), severe in 1 patient, but this lady probably has a primary psychosis. It is noted that in 2 patients there were severe mental changes after direct obliteration of the aneurysm. Also, after this latter procedure an oculomotor palsy developed in 3 patients.

There were 4 deaths with evidence of brain-stem ischaemia in patients who had bled 2, 3, 14 and 42 days prior to carotid artery ligation, and who survived for 1, 1, 6 and 1 day(s) respectively. Each patient was critically ill when treated. Autopsies showed acute swelling of the ipsilateral cerebral hemisphere. Two other patients died within 36 hours of carotid artery ligation, but both were treated in 1936; autopsy was performed in one of these cases, in which a postoperative hemiparesis had developed, and the findings were similar to those described above. Another patient who was very ill from his fourth haemorrhage, had his fifth and fatal haemorrhage during occlusion of the internal carotid artery by a clamp. In 1 patient treatment had consisted only of evacuation of a large temporal lobe haematoma, but 11 days after his first bleeding, he had a massive fatal haemorrhage.

Direct approach to the aneurysm may be obtained conveniently through a subtemporal craniectomy (Fig. 6). Lumbar drainage set up at the beginning of the operation will facilitate exposure of the aneurysm, and it is wise to have the ipsilateral internal carotid artery in the neck under direct control, by passing a wide tape around it. The fields of the head and the neck are included in the same draping of the wound. It is sometimes necessary to include the posterior communicating artery in the clip, with no ill effects. During this intracranial approach to these aneurysms different degrees of spasm of the involved arteries have sometimes been observed. It has been found that a 2.5 per cent solution of papaverine applied locally by means of small cottonoid pledgets will release this spasm, usually within a few minutes. This procedure has been adopted in Edinburgh during the past few years. On Professor Dott's suggestion, if the spasm has tended to recur at operation, a fine polythene tube has been left in place, and $\frac{1}{2}$ cc. of a 2.5 per cent solution of papaverine has been injected through this tube 6 hourly for 24 hours.

Unfortunately the fundus of the aneurysm usually points laterally, and especially if the lesion is sessile, it may only be possible to wrap it with crushed muscle. Jefferson[6] considers that all or nearly all aneurysms

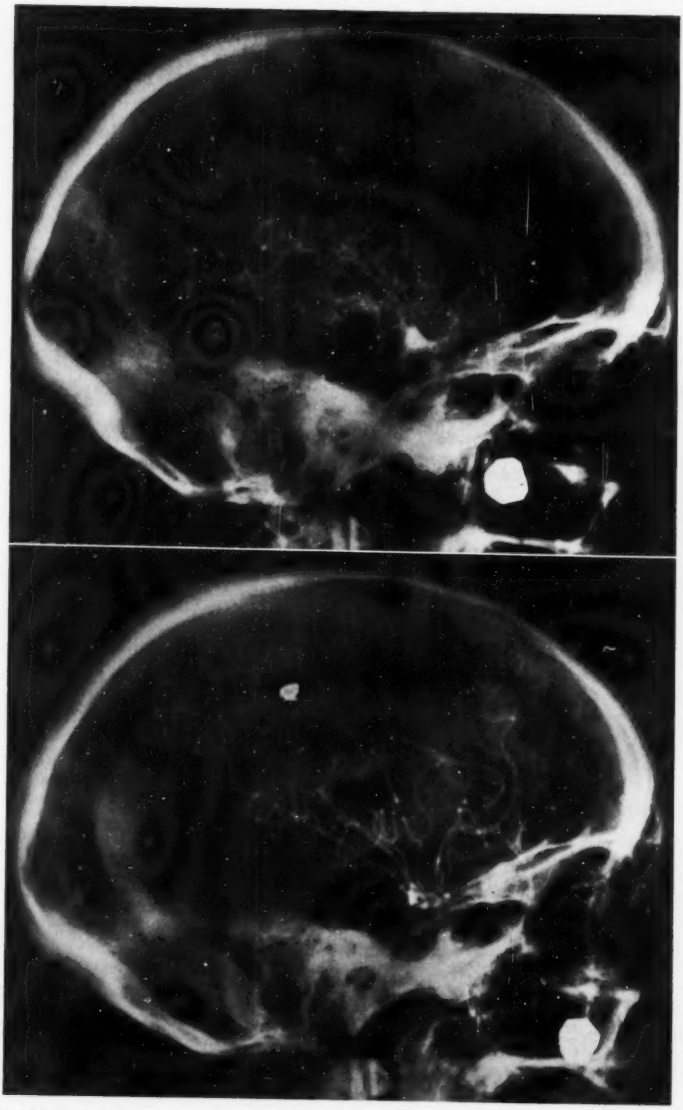

FIG. 6. (*Above*) Angiogram showing an internal carotid-posterior communicating artery aneurysm, and (*below*) postoperative angiogram after a direct approach for obliteration of the aneurysm by a silver clip applied to its neck.

are sessile, and that the neck of an aneurysm is too often a radiological appearance. Some surgeons[7] prefer to ligate the internal carotid artery in the neck and later to clip this vessel distal to the aneurysm.

One patient had a further bleeding 7 days after the aneurysmal neck was clipped (Fig. 6). Repeat angiography showed no evidence of the lesions, and therefore it was presumed that leakage of blood had occurred from a weak area in the occluded neck of the aneurysm.

It may be seen that there are complications with either form of treatment (Table 2), but with better selection of cases, and with the aids of hypothermia and hypotension fewer serious complications should be seen.

Some speculation may be made regarding the choice of operation: thus proximal ligation of the carotid artery is suitable when there is a good anastomotic circulation, if the aneurysm is large, and/or sessile. The direct procedure is required when the anastomotic circulation is poor, when there is a contralateral (or ipsilateral above the bifurcation of the internal carotid artery) aneurysm, if the aneurysm fills on testing the contralateral anastomotic circulation. A small aneurysm, with an inviting neck, is suitable for the intracranial operation.

FOLLOW-UP STUDIES

Much has to be learnt about the natural history, and also the long-term results of treatment in patients with intracranial aneurysms. In this series, 12 patients have been followed up for over 9 years, another 5 for over 5 years, and a further 17 for over 2 years. One patient, who had severe hypertension, died 18 months after ligation of the common and internal carotid arteries. One died many years after treatment, which consisted of ligation of the internal carotid artery done in 1935. Another patient, who did not have surgical treatment, died 6 years after investigation. The cause of death is not known in these 3 patients.*

SUMMARY

The angiographic appearances of 90 patients with aneurysms arising at the junction of the internal carotid and posterior communicating arteries are described, and in 84 the clinical syndromes are discussed.

Some indication is given for the timing of angiography, and for surgical treatment.

The significance of arterial spasm, and of arterial hypotension, is stressed.

Angiographic and clinical follow-up are very important.

A more critical method of testing the anastomotic circulation is given, and some criteria for the type of operation are stated.

We wish to acknowledge with gratitude the valuable help given to us by Professor Norman M. Dott in the preparation of this paper.

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SPONTANEOUS HEMATOMYELIA AND ANGIOMAS OF THE SPINAL CORD

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THE term spontaneous hematomyelia has been used for a number of years to describe the sudden onset of pain and rapid development of long tract signs in a previously asymptomatic individual. Although numerous cases have been reported, the etiology in most instances has been obscure. Syphilis, spinal cord tumors, myelitis, hemorrhagic diathesis, aneurysm, angioma, and trauma have been listed as the various causes of intramedullary bleeding. Hematomyelia caused by angiomatous malformations has been reported by Richardson,[11] Buckley,[2] Gatenby,[6] Wyburn-Mason,[14] Hieke,[9] and Vraa-Jensen.[13] In 1938, Richardson,[11] in discussing the etiology, stated "intramedullary vascular tumors and malformations may eventually prove to be the commonest cause with syphilis, acute myelitis and arteriosclerosis contributing a smaller share." The significance of this statement seems to be confirmed by the fact that in all 3 cases of hematomyelia that we have encountered the cause of the bleeding was proven to have been small angiomatous malformations. For this reason, the following cases are reported and the syndrome is compared to that of extramedullary vascular malformations.

HEMATOMYELIA SECONDARY TO INTRAMEDULLARY ANGIOMA

Case 1. E.J., a 35-year-old white female, was admitted to Duke Hospital on Mar. 6, 1950. In January 1950, she had first noted numbness of the thumb and index finger of the left hand, followed by severe pain in the neck. The pain continued until March, by which time progressive weakness and numbness of all extremities had developed.

Examination revealed generalized weakness, more marked in the lower extremities and left arm, impairment of sensation to C6 and increased deep reflexes. Roentgenograms of the spine, manometric studies and myelogram showed no abnormalities.

Course. Her condition gradually improved and by August 1950 she was able to get around on crutches.

In October 1950, there was an increase in her numbness and weakness and she had difficulty in voiding, which gradually progressed.

Readmission, Dec. 6, 1950. Examination revealed marked weakness of all extremities with a flaccid paralysis of the left arm. The sensory level extended up to C5. The cerebrospinal fluid was clear and colorless, contained no cells, and total proteins were 52 mg. per cent. Manometric findings were normal but myelography revealed enlargement of the cervical cord.

Operation. Cervical laminectomy, C2–C6. The cervical cord was enlarged and there was an area of bluish-purple discoloration in the posterior column on the left, extending from C3 to C4. An intramedullary hematoma was evacuated, leaving a cavity from C3 to C5. Several small vessels were encountered entering the hematoma. There were no abnormal vessels on the surface of the cord and there was no evidence of subarachnoid hemorrhage.

Pathological Report. Tissue removed from the wall of the hematoma revealed a number of vessels of various sizes, the walls of which were composed of a single endothelial layer. Some of the vessels were grouped together with their walls intact while others were separated by hemorrhagic cord tissue (Fig. 1).

FIG. 1. *Case 1.* Operative specimen removed from wall of hematoma. Thin-walled vessels of various sizes in groups and separated by hemorrhagic cord tissue. Hematoxylin and eosin, ×70.

Postoperative Course. There was improvement in motor function which gradually progressed for several months.

Readmission, Nov. 7, 1951. She was readmitted because of the sudden onset of pain low in the back and in the left leg, of 3 weeks' duration. Neurological findings at this time were weakness of the left arm, good motor function of the lower extremities, decrease in all sensory modalities from C5 down, and bilateral plantar extension. Myelography revealed a defect in the lower lumbar region.

2nd Operation. Laminectomy, L5, revealed an ependymoma. A subtotal resection of the tumor was carried out.

Postoperatively, she was given a series of roentgen-ray therapy.

Case 2. V.L.T., a 33-year-old colored female, was admitted to Duke Hospital on Sept. 17, 1953. Four days previously, severe pain had developed in the right arm and, shortly afterwards, less severe pain in the left arm. On the second day, there

were weakness and numbness of both legs and, on the third day, she was unable to void or defecate.

Examination revealed marked weakness of the lower extremities, slight generalized weakness of the upper extremities and a sensory level up to T4. Roentgenograms of the spine were negative. Lumbar puncture revealed normal manometric findings; cerebrospinal fluid contained 5 white blood cells, and total proteins were 60 mg. per cent. Myelogram showed a questionable widening of the cervical cord.

The weakness gradually progressed and she expired on the 10th hospital day.

Autopsy. The gross findings of importance were confined to the spinal cord. There was an extensive intramedullary hemorrhage extending throughout its length. In the upper thoracic region, there was a fusiform swelling where the cord was twice its normal size. Cross section of the cord revealed that the hemorrhage had dissected through the posterior column up to the medulla and down to the lower lumbar region (Fig. 2). There was no gross vascular abnormality and there was no subarachnoid hemorrhage.

Microscopic examination revealed an angiomatous malformation in the posterior column of the area of C5 which extended rostrally about 1 cm. Its transverse diameter measured approximately 4 mm. It consisted of numerous tortuous vessels with irregular lumens. The walls of the vessels were composed of connective tissue in which no muscularis or elastica could be seen (Fig. 3).

Case 3. N.L., a 12-year-old white female, was admitted to Duke Hospital on April 13, 1954. Three days previously, she had sudden onset of pain low in the back and in the right leg. The pain in the right leg became progressively more severe during the next 2 days and, at this time, a dull aching pain developed in the left leg. Three days after the onset, she noted weakness of the right leg which progressed to almost complete paralysis by the 4th day. On the 5th day, the pain in the left leg became more severe and, at this time, marked weakness of the left leg developed. She had not had a bowel movement for 3 days and, on the morning of admission, urinary retention developed.

Examination revealed weakness of both legs, but more marked on the right, absent knee and ankle jerks, and bilateral plantar extension. Sensory examination was difficult to evaluate but there seemed to be a hyperesthesia over the entire right leg. Slight passive movement of either leg produced severe pain in the corresponding extremity. Roentgenograms of the spine were negative. Lumbar puncture, on the 6th day of illness, revealed a pressure of 120 mm. water, 40 white blood cells, and 5,000 red blood cells, with total proteins of 64 mg. per cent, and xanthochromic supernatant fluid.

Course. During the next 2 days, her condition improved but on the 8th day, her pain returned and weakness increased. Myelogram revealed a partial block at L1.

Operation. On April 21, 1954, a lower dorsal, upper lumbar laminectomy was performed. The cord at the level of L1 was swollen and there was an area of bluish-black discoloration on the right side. There were no abnormal vessels on the surface of the cord. An incision was made through the discolored area and an intramedullary hematoma was evacuated.

Pathological Report. Tissue dissected from the wall of the hematoma on the right side revealed numerous vessels of various sizes. The walls of the vessels varied in thickness from a single layer of reticulin to dense collagen (Fig. 4).

Postoperative Course. The pain subsided immediately and there was gradual but marked improvement in motor and bladder function at the time of discharge 4 weeks following operation.

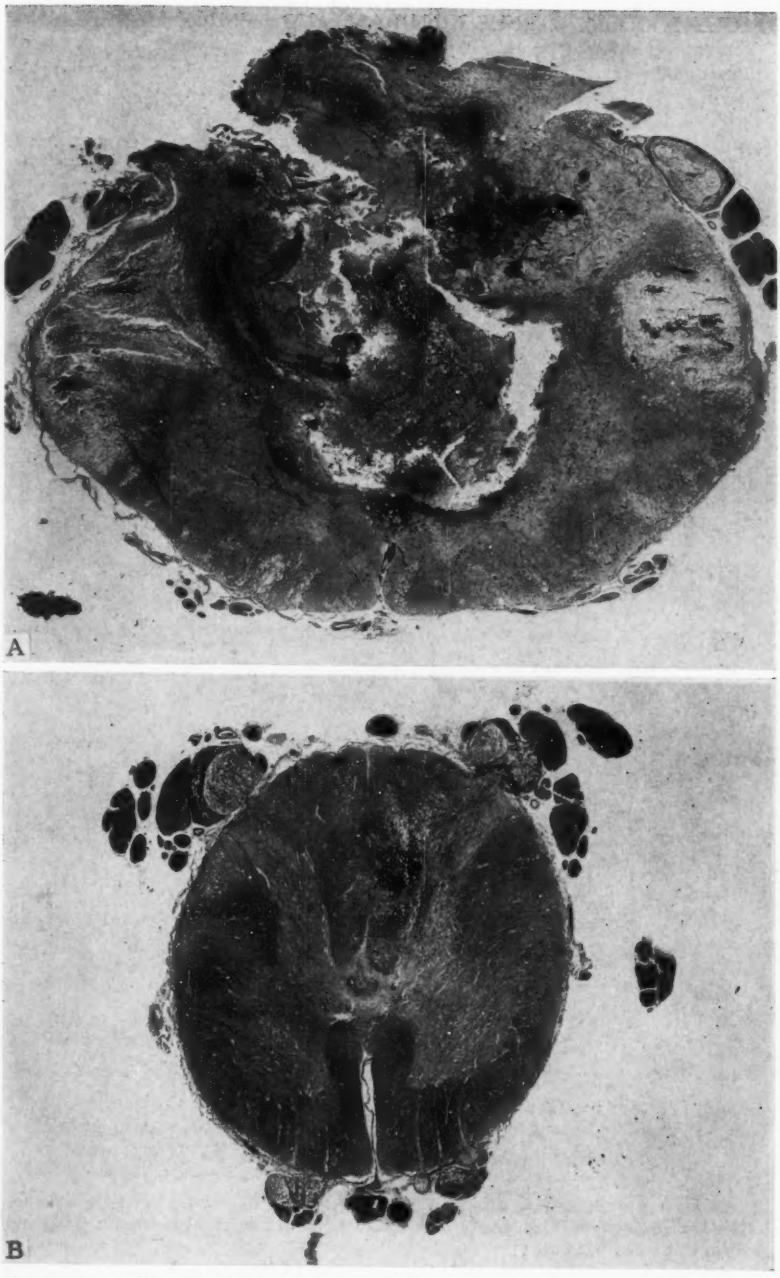

FIG. 2. *Case 2.* (A) Cervical cord. Collection of abnormal vessels in posterior column adjacent to hemorrhage. (B) Lumbar cord, revealing lower extent of hemorrhage in posterior column. Hematoxylin and eosin, ×81.

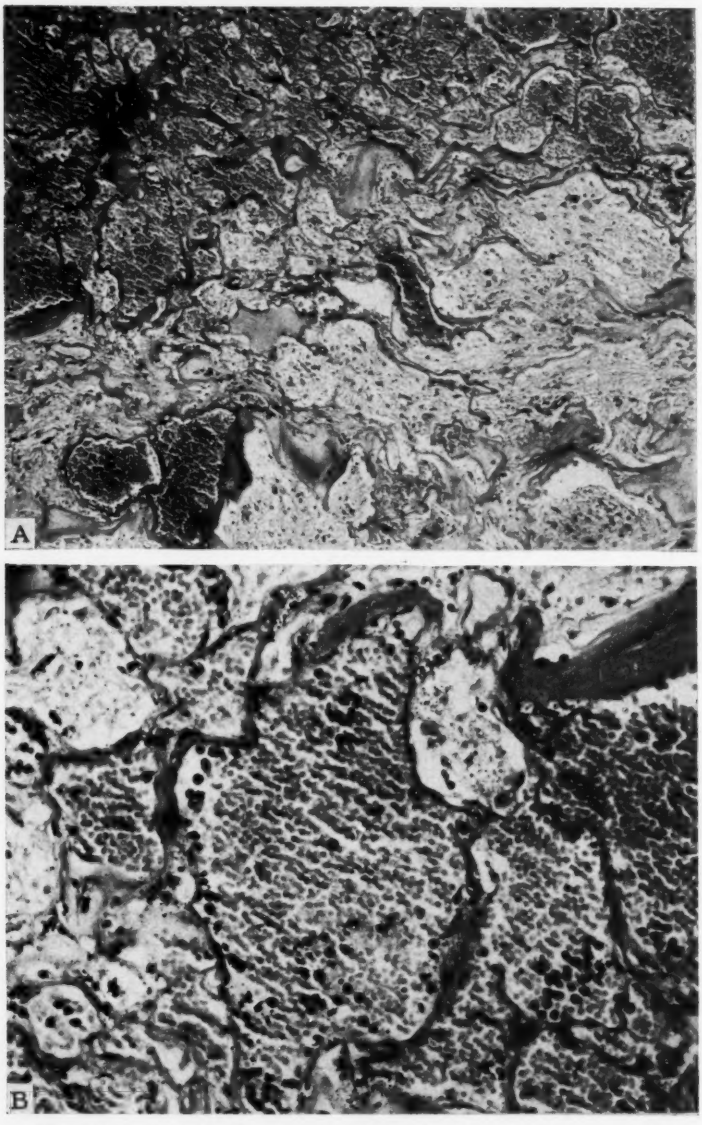

FIG. 3. *Case 2.* (A) Section taken from posterior column, level of C5. Numerous vessels with irregular lumen. Hematoxylin and eosin, ×70. (B) Thin-walled vessels, without muscularis or elastica layer. Hematoxylin and eosin, ×236.

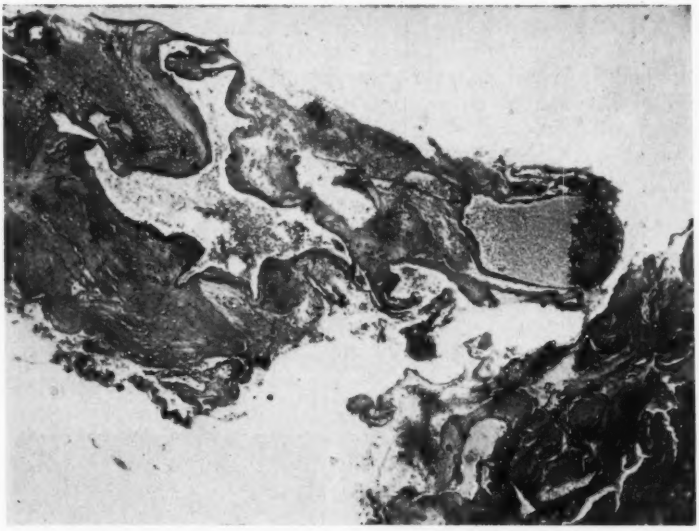

FIG. 4. *Case 3.* Operative specimen removed from wall of hematoma. Vessels of various sizes, with thin walls varying in thickness from single layer of reticulin to dense collagen.

EXTRAMEDULLARY ANGIOMAS

Case 4. L.D., a 46-year-old white female, was admitted to Duke Hospital on Feb. 18, 1947. Two years previously, she began to have aching pain in the left hip and leg, followed by gradual development of numbness of the left leg, and then the right. Shortly after the onset of the numbness, she began to have weakness in both legs. A negative exploratory lumbar laminectomy was performed, at another hospital, in 1945. Strength gradually returned in her legs and the pain subsided.

In April 1946, she fell to her knees and, since then, had been unable to walk. At this time severe pain developed low in the back and in both legs, with incontinence of urine and feces. During the last 2 months, there had been slight improvement in the strength and less numbness.

Examination revealed marked spastic paraplegia with absent deep reflexes in the left leg and hyperactive reflexes on the right, and a sensory level to T8. Roentgenograms of the spine revealed absence of the spines of the first three lumbar vertebrae with retained oil. Myelogram was not satisfactory because oil could not be pooled in the dorsal region. Total proteins of the spinal fluid were 116 mg. per cent.

Operation. On Feb. 26, 1947, a dorsal laminectomy of D5 through D8 was performed. When the dura mater was opened, a vascular malformation was disclosed over the posterior surface of the cord, extending from D4 to D10. This proved to be one vessel which was extremely tortuous, with the loops in close proximity, the rostral end leaving the canal through the left intervertebral foramen between D6 and C7. Several of the loops of the vessel floated free in the subarachnoid space and others were adherent to the posterior surface of the cord. The vessels were removed by sharp dissection after clipping the caudal and rostral ends. Following removal, the cord appeared slightly yellowish but normal in size.

Postoperative Course. There has been some decrease in spasticity and definite decrease in pain, but she has continued to be completely incapacitated.

Case 5. H.E., a 19-year-old white male, was admitted to Duke Hospital on July 18, 1951. Three weeks previously, he began to have pain in the left side of the chest which gradually increased in severity and became girdle in type. The pain was aggravated by standing and relieved by lying down. Several days after the onset of the pain, he noted weakness of the left leg and numbness of the right.

Examination revealed a weakness of all muscle groups of the left leg, impairment to sensation over the right leg and right side of the abdomen to the level of the umbilicus, and hyperactive deep reflexes in the lower extremities.

Roentgenograms of the spine were negative. Myelogram revealed a tortuous worm-like defect throughout the dorsal region (Fig. 5). Total proteins of the spinal fluid were 64 mg. per cent.

Operation. On July 25, 1951, dorsal laminectomy, D6–D8, was performed. The posterior surface of the cord was covered by a number of large tortuous thin-walled vessels and the cord was symmetrically enlarged about twice its size. There was no evidence of hemorrhage and no attempt was made to aspirate or incise the cord. The dura mater was left open.

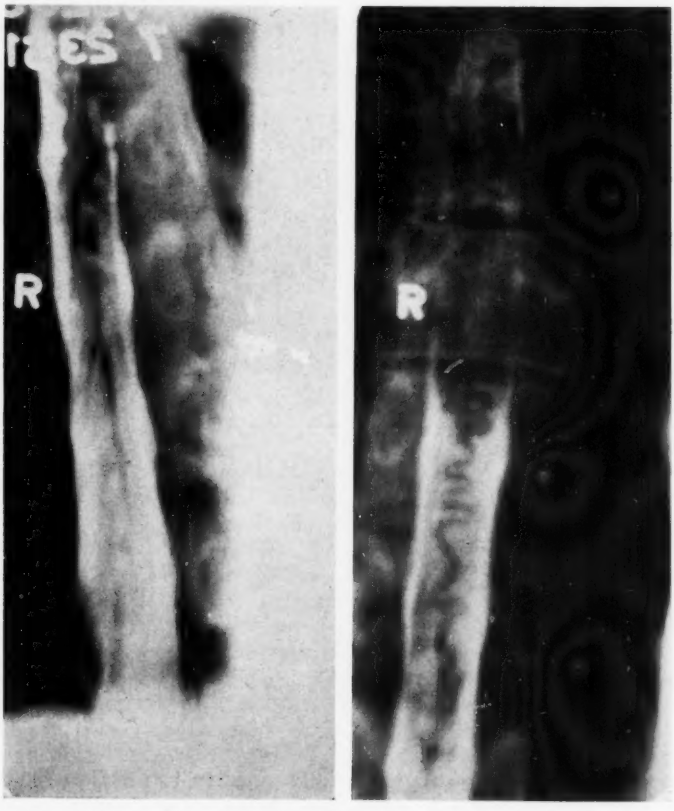

FIG. 5. *Case 5.* Typical myelographic defect produced by anomalous vessels throughout dorsal region.

Postoperative Course. A series of roentgen-ray therapy was given. Following operation, there was additional weakness of the right leg which gradually improved and within several weeks, his strength was better than before operation. Since then, slight weakness of the left leg and numbness of the right thigh have developed.

Case 6. R.B., a 39-year-old white female, was admitted to Duke Hospital on April 16, 1953. Seven years previously she began to suffer from paresthesias of the right hand and pain in the neck, which were followed by clumsiness, and then by weakness and spasticity of the right arm and leg. The diagnosis of multiple sclerosis was made in 1948. There was gradual progression of these symptoms without remission and, in 1953, burning pain developed in the left thigh, which was not influenced by change in position.

Examination revealed spastic weakness of the right arm and leg; hyperactive deep reflexes which were slightly more active on the right; and ankle clonus, sustained on the right and transient on the left. Right plantar response was extensor; left was equivocal. Sensory abnormalities consisted of mild impairment of two-point sensation and recognition of objects in right hand and vibration in right foot. There was no impairment of sensation to pin prick.

FIG. 6. *Case 6.* Cervical myelogram revealing large irregular filling-defect produced by extramedullary vessels shown in Fig. 7.

Roentgenograms of the cervical spine were negative. Manometric findings were normal. Total proteins of the spinal fluid were 37 mg. per cent. Myelogram revealed an irregular, tortuous (serpentine) filling defect in the cervical region extending from C2 to C7 (Fig. 6).

Operation. Cervical laminectomy, C3–C7, revealed a large collection of vessels mainly on the right side of the cord from C2–C7. The vessels varied from 1 mm. to 4 mm. in size, were thin-walled and extremely tortuous, and appeared to contain arterial blood (Fig. 7). The cord and malformation were decompressed by leaving the dura mater open.

Course. Immediately after operation, there was slight additional weakness of the right arm and leg, but strength was regained in several weeks. During the past 6 months, there has been slight progression in the spasticity and weakness of the

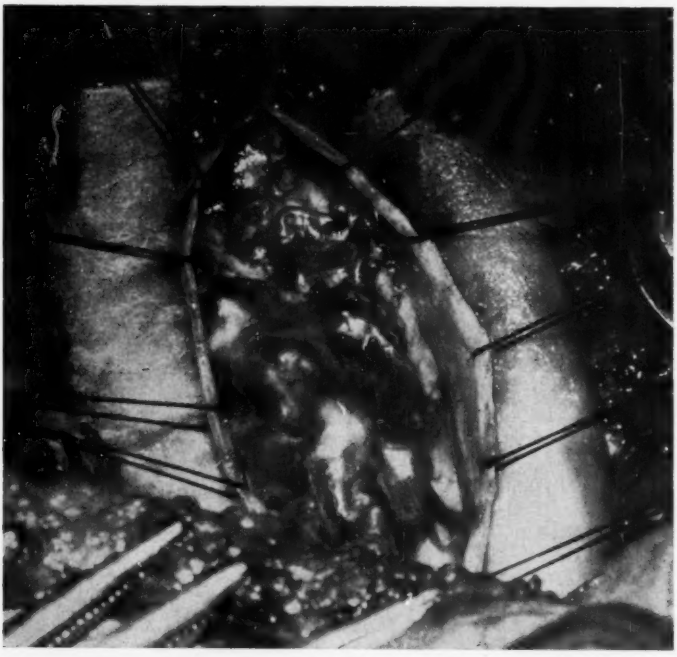

FIG. 7. *Case 6.* Cervical arteriovenous angioma. Vessels vary in size, and are tortuous and thin-walled.

right arm and leg and she has noted numbness of the left side of her body. Two series of roentgen-ray therapy were given postoperatively.

Case 7. J.A.P., an 11-year-old colored female, was admitted to Duke Hospital on Nov. 15, 1954 with chief complaint of severe headache. Four days before admission, she had suddenly lost consciousness for 2 to 3 minutes. This was followed by severe frontal headache and impairment of vision in the left eye. The visual complaint subsided in 20–30 minutes.

At the age of 2 years, she had an illness which was diagnosed as whooping cough, during which she had a convulsive seizure, followed by a right hemiplegia. The hemiplegia persisted but she had no further convulsions. Further detailed information could not be obtained in regard to this illness.

Examination revealed marked stiffness of the neck, and weakness of all extremities, more marked on the right. There was spasticity of both legs, a left ankle clonus, and bilateral Babinski sign. There was no definite sensory abnormality.

A lumbar puncture, on November 18, revealed a pressure of 260 mm. of water and the cerebrospinal fluid was grossly bloody. Bilateral cerebral arteriograms failed to reveal an angiomatous malformation or aneurysm. A cervical myelogram showed a tortuous filling-defect from C3 to C7, with a large central round defect at C7.

A diagnosis of arteriovenous angioma of the cervical cord with subarachnoid hemorrhage was made. The lesion was not explored. Her condition gradually improved but at the time of discharge on Nov. 30, 1954, she still had bilateral weakness, which was more marked on the right side.

Comment. The failure to obtain an accurate report of the child's illness at the age of 2 proved to be misleading. It was at first thought that she had pertussis encephalitis because of the history of a seizure followed by right hemiplegia, the febrile illness having been diagnosed as whooping cough.

While in the hospital, a record of her illness of 1945 was obtained and this revealed not only weakness of the right arm and leg but slight weakness and spasticity of the left arm and leg with bilateral Babinski sign (diagnosis: poliomyelitis). It was because of this information and the bilateral cord signs that a cervical angioma was considered and myelography was done.

DISCUSSION

Vascular malformations of the spinal cord are considered rare as compared to similar lesions of the brain. In part, this may be attributable to the fact that they go unrecognized unless accidentally encountered at operation or post mortem. This is especially true in cases of hematomyelia, as in cases of spontaneous intracerebral hematomas (Margolis *et al.*[10]), in which the lesion frequently is not proven except at the microscopic level.

These vascular malformations produce two distinct clinical syndromes. The first is that of spontaneous hematomyelia secondary to small intramedullary angiomas (Cases 1, 2 and 3), which is characterized by the sudden onset of severe pain and rapid development of long tract signs in a previously asymptomatic individual. The second is caused by extramedullary venous or arteriovenous angiomas (Cases 4, 5, 6 and 7), in which there is a gradual or sudden onset of pain of root type followed by gradual development of long tract symptoms and signs. The symptoms usually improve but are followed by relapses with more neurological deficit than the previous episode.

The intramedullary angiomas tend to occur in the posterior columns of the cord and consist of a fairly localized collection of vessels which vary in size. The pial vessels are not involved. If bleeding occurs, it is usually confined to the cord and does not extend into the subarachnoid space. In Case 3, however, there were 5,000 red blood cells in the cerebrospinal fluid. The resulting hematomyelia may extend in both directions from the lesion and involve the entire length of the cord, as in Case 2.

The cerebrospinal fluid may be clear and colorless or xanthochromic, with increased total proteins and some degree of block of the subarachnoid space by manometric testing or by myelogram.

The early recognition of this syndrome seems essential because evacuation of the hematoma may prevent further extravasation of the blood and more extensive cord damage. The fact that these lesions seem to be confined to the posterior columns simplifies recognition of the lesion at operation and evacuation of the clot.

The extramedullary venous and arteriovenous angiomas are encountered predominantly in the cervical and dorsal regions of the cord. Skin nevi may occasionally be associated with these lesions[3,4,7,12,14] and, when present, prove to be of definite diagnostic value.

In contrast to the intramedullary angiomas, the extramedullary venous

or arteriovenous angiomas may bleed into the subarachnoid space as well as into the cord. The spinal subarachnoid hemorrhage may be so profuse that it may be confused with intracranial subarachnoid bleeding, as in Case 7. In the former, there is usually evidence of cord involvement which should make one suspect the presence of a spinal angioma. The neurological progression and remissions in these cases are thought to be caused by thrombosis of vessels in the intramedullary portion of the lesion,[8,13,14] rather than by hemorrhage. Hematomyelia secondary to an extramedullary arteriovenous angioma has been reported by Wyburn-Mason.[14]

Manometric studies in our cases failed to reveal an obstruction in the subarachnoid space but a block has been recorded by Cross.[4]

The myelogram may show a classical picture, as shown in Fig. 5, in which there is a tortuous serpentine defect over several segments of the cord. These changes have been reported by Epstein *et al.*[5] and by Bassett *et al.*[1] This typical finding may not be present if there is a complete block in the subarachnoid space.

Surgery has but little to offer in the cases of extramedullary angiomas and does not seem to alter the course of the syndrome. This has been true of our cases and all that have been reviewed in the literature. Decompression, removal or coagulation is not beneficial because the lesion is not only extramedullary but intramedullary as well. If pain is an outstanding complaint, it may be decreased by decompression. Roentgen-ray therapy has also been used without improvement.

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RESPONSIBILITY FOR DIAGNOSIS IN THE "BRAIN TUMOR SUSPECT"*

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ANY mention of medical records nowadays is apt to provoke a sour grimace. This conditioned response has been developed by the monotonous insistence of hospital record-librarians that doctors must complete their hospital charts according to the book.

It is less irritating, and more rewarding, to be critical of one's own office records. Standards for the medical files of private practice are self-imposed. The accepted pattern for a neurosurgeon is a cross-index system and rigidly objective records. One sets the gauge at the very beginning. The subsequent course is like the fable of the old man who would not get off Sindbad's back. When the load has been accepted it is yours for life.

TABLE 1

Total series of "Brain Tumor" cases

Brain tumor verified		333
Brain tumor unverified		149
Brain tumor suspect		558
Total		1040
Epilepsy (sole complaint)		822
Adults	423	
Children	399	
Headache (sole complaint)		374

After one has completed two decades of specialty work in medicine it is a salutary and humbling experience to glance back at the notes that one has made on the way. Three years ago an analysis of the author's office files revealed that there had accumulated the cross-indexed records, more or less complete, of 10,000 cases (plus a few hundred) in 20 years of private practice as a neurosurgeon. Roughly one-tenth of these cases, 1,000 patients, were listed as "Brain Tumor" (Table 1).

Diagnoses were attached to the record and filed, usually within 1, and seldom more than 2 weeks, after the first examination. There is no need to

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specify any operational definition of "Brain Tumor Verified," "Brain Tumor Unverified" or "Brain Tumor Suspect." "Epilepsy" applies to patients with seizures in whom one suspects some cause other than brain tumor for reason of age, long history, or because of the nature of the attacks.

Some patients with a sole complaint of headache, who are sent to a neurosurgeon, do not present a remote suggestion of brain tumor in their story or on neurological examination. These are the cases of postural fatigue, anxiety tension states, headaches from arterial hypertension, cerebrospinal hypotension, etc. They are not added to the files of the "Brain Tumor Suspect" and are recorded as plain "Headache." Others come with headache of a more ominous type—sharp, frightening pains, deep aches that persist and worsen, early morning headaches, etc. These cases, even with a negative neurological examination, are listed "Brain Tumor Suspect."

TABLE 2

Total cases of "Brain Tumor Suspect"

1. Lost		90
2. Absence of tumor established		364
3. Brain tumor verified		85
(a) in 1 month or less	62	
(b) in over 1 month	23	
4. Still under observation		19
Total		558

"Brain Tumor Suspect" is an artificial category. It will be differently employed according to the type of one's medical practice. Every patient who is eventually treated for brain tumor must have been a suspected case for some doctor at some time. All of the patients whose records are reviewed in this report (Table 2) were referred for examination by a non-neurosurgical colleague. He usually had not hazarded any diagnosis, but thought that the total situation justified investigation by a neurosurgeon. The responsibility for establishing a satisfactory final diagnosis is the principal reason for the tag "Brain Tumor Suspect," or so it has been somewhat loosely accepted by the author over the years. If the principal reason for referring such a patient to a neurosurgeon is to establish or to rule out the diagnosis of tumor, what happens when neither can be accomplished? Who becomes responsible for ensuring that the problem will be pursued—the patient, his relatives, the neurosurgeon, or the referring doctor?

The 90 patients with whom all contact was lost is a disconcerting group to consider. It might seem incredible that almost 1 in 6 of patients who had such a potentially serious diagnosis could drop out of sight. However, many of them are presumed to have rightfully returned to the referring doctor—e.g. to a general practitioner or internist for management of arterial hypertension, obesity, cerebral arteriosclerosis, etc., or to an ophthalmologist for further observation of ocular imbalance, hemianopia, optic atrophy,

etc. or to an otologist for observation and management of loss of hearing, tinnitus, etc., or to a neuropsychiatrist for follow-up for their anxiety state, obsessional trends, deteriorated behaviour, etc. In the course of time, these conditions were presumably resolved, and the patient was discharged. But at what stage is the suspicion of brain tumor finally disproved, and by whom?

It is easier to arrange for recheck of a patient who has been carried through a serious illness or operation, than of one who has been the subject of a "negative" investigation. Perhaps we have emphasized follow-up examination on the wrong group of patients. Whether or not a recheck of the "Brain Tumor Suspect" is apt to be fruitful, it is apparent that he cannot be discharged in the conventional manner. He may be freed to resume his travels but he has been unknowingly relieved of his passport of good health.

It is noteworthy that there was no tendency for children, who had been placed in the "Brain Tumor Suspect" group, to become lost. Out of 46 children under the age of 18, only 1 was not followed to the stage of complete diagnosis. No age trend is apparent in the adult cases. In a few of the old people the record played out, even though further special tests appear to have been indicated. Sometimes, in old age, when the initial neurological examination was negative, it was decided that further investigation would just be meddlesome. The merits of that attitude may be questioned. Scattered through the records are a few cases of elderly patients about whom one had second thoughts, and found a subdural hematoma or a benign curable tumor. There is no consistent reason for placing the old folk in a special category.

Absence of Tumor Established. The criteria for accepting that 364 patients have had the absence of tumor established might be debated in some instances. An assessment of what constitutes adequate follow-up has involved experience and judgment, which the ancient Greeks told us are perilous and fallacious. The experience of patients seen in the first 10 years has been used in a further 10 years of retrospect, to judge the adequacy of records in those second 10 years. In a relatively circumscribed medical community such as British Columbia, with only a few neurosurgeons, all but one in the same city, mistakes and near misses in the diagnosis of lethal disease, such as brain tumor, nearly always come to their perpetrator's attention. Alternatively, in a considerable number of cases, a request years later from an insurance company for evidence of insurability establishes that as far as brain tumor is concerned, the patient's passport of health can be returned.

Technical tests such as pneumoencephalography, arteriography, electroencephalography and isotope studies can be a great help to eliminate tumor. They are so impressive that when they yield negative results, both patient and referring doctor, and sometimes the neurosurgeon, may be lulled into a false sense of security.

Pneumoencephalography has been variously employed and variously

performed through the years that are covered by this survey. During the early forties it was learned with some dismay, that a negative pneumoencephalogram, though it supplied important evidence, does not invariably eliminate brain tumor. This did not always prove to be a serious miss from the patient's viewpoint. It sometimes preserved him from useless surgery. The tumor in those cases was usually glioma.

Brain Tumor Verified. Brain tumor did develop in 85 patients of the total group, roughly 1 in 5 of the cases that were followed. In 62 of these cases the diagnosis was established within a month. Leaving this group within the "Brain Tumor Suspect" category in my files is arbitrary. It usually signifies that they were classified after neurological examination, and before any special tests had been employed.

The remaining 23 verified cases are more important. The average patient in this group did not have the existence of brain tumor established for 18 months. The longest elapsed time was 7 years. In 9 of these "delayed action" cases the patients had a presenting complaint of fits. All but 1 were eventually proven to have an astrocytoma. They had suffered fits for an average of 10 months when they first arrived for neurosurgical attention. The tumor was not disclosed until an average of 30 months later. So they went over 3 years from the onset of symptoms until discovery of tumor. There is not much doubt that in some of these cases a repetition of pneumoencephalogram, or arteriography, or the use of isotopes, with which the author's experience has been meagre, might have disclosed the tumor at an earlier date. That is true for the one meningioma that somehow went unrecognized for a year. Except for the relief of headache, there is little evidence that the remainder, who had gliomata, were any better off after operation than before. Even the fits continued in nearly all of them.

Further consideration of this small but important group led to an investigation of the records of patients who had been filed under the diagnostic title of "Epilepsy." Could one's index of suspicion be so low that a brain tumor might turn up here? They had been filed as epilepsy after preliminary investigation, which usually included pneumoencephalography and electroencephalography, had drawn a blank. This search disclosed 7 more brain tumors, all astrocytomas, with an average delay in the diagnosis of tumor of 3 years from the time of the first neurosurgical examination, and 7 years from the onset of symptoms.

One patient, aged 48, at the time of his death from astrocytoma in 1955, had suffered focal seizures affecting his speech, arising at the site of his tumor, for 20 years. In 1940, about 5 years after the onset, when the author first examined him, he had already been examined by six leading North American authorities on epilepsy. His tumor was disclosed at operation 12 years later.

The question arises: Should one explore when there are continued focal seizures with localizing neurological signs and/or localizing electroencephalographic evidence, but a normal pneumoencephalogram? Nowadays the additional evidence of arteriography and/or isotope studies would be on

hand to help in such a decision. Nevertheless, when the neurosurgeon does explore in the early stages of glioma the findings can be very puzzling.

Mr. B., aged 42, came for examination in August, 1947. For 3½ years he had suffered focal seizures several times per day. His right fingers would flex convulsively and then he would become speechless. At intervals of about 6 months convulsive movements during an attack would spread to his shoulder and then he would lose consciousness. Neurological examination and pneumoencephalogram at Liverpool, England, a few months earlier, were reported negative. He had no abnormal signs. Electroencephalogram was "normal." Six months later he had repeated bouts of status epilepticus for several days. These did not respond to any of the standard methods of treatment. It was decided to explore. A large, left frontoparietotemporal bone flap was turned. Appearance of the brain was entirely normal except for a pronounced appearance of congestion of cortical vessels in the pre- and postrolandic arm area. Nothing abnormal was felt with exploring brain needle.

He recovered from operation and from his epileptic status, but periodic fits went on as before, though less frequent. He continued to work steadily and support himself. In November, 1955, 8 years after the first examination, 11 years after his first fit, he returned with a new complaint of headache. Pneumoencephalogram and arteriogram showed a mass in the center of the left frontal lobe. Again he was explored. Intracranial pressure was only slightly increased. The cortex appeared normal. There was abnormal resistance to the exploring needle throughout the whole center of the lobe. A biopsy of this tissue was reported negative for tumor. In spite of the biopsy, though with some misgivings, the area was resected. Proper sections then identified the tissue as astrocytoma, Gr. 1.

One might say that this man had almost remained a "Brain Tumor Suspect" even after the neurosurgeon had looked at the tumor area twice!

It is interesting to compare epilepsy with headache as the sole presenting symptom. In those instances of this series of "Brain Tumor Suspects" in which headache was the complaint and tumor did exist (17 cases) the final diagnosis was established within a month, in contrast to the epilepsy group where the tumor could remain hidden so long. It seemed prudent to go back to the general files again and determine whether follow-up revealed any unpleasant surprises in patients who had been filed under the symptomatic diagnosis of "Headache" with no suspicion of tumor. None of the 374 has so far shown up with brain tumor. Danger of misclassifying does not seem to lie in that direction.

The majority of the "Brain Tumor Suspects," roughly 5 out of 6, came with a solitary complaint: such as fits, headache, mental confusion, failing vision or advancing deafness. Usually they would have no more than one abnormal sign, such as blurred discs or facial weakness, an electroencephalogram with predominance of unilateral abnormality, nerve deafness or hemianopia, etc. Twenty-one proved to have pneumoencephalographic evidence of cerebral atrophy. The symptoms in this group were diverse—failing vision, hemiparesis, fits, poor memory, etc. Patients with unilateral deafness, usually associated with tinnitus and/or dizziness, were always suspected of having an acoustic neuroma. Early diagnosis of this tumor must

require a lot of negative searching. None of the patients that the author examined with acoustic neuroma in mind, whose abnormal signs were limited to the 8th nerve, turned out to have tumor; and yet they must occur. At the beginning, these patients just do not complain, or, if they do, the mild and relative nature of the deafness is not regarded seriously.

Visual complaints, with abnormal signs restricted to the visual apparatus, were common. Of 88 "brain tumor suspect" patients whose complaint was only in respect to vision, tumor was verified in 11. Usually the presence of tumor was established without difficulty. But there are obscure lesions around the optic chiasm that simulate tumor, notably aneurysm and some tumors of the orbit, when decision may require a careful period of observation and repeated examination. One of these cases in the visual-loss group illustrates the disaster that can overtake a patient when the necessity and the means of follow-up examination are not clearly established.

This man, aged 55, while asleep, suffered total loss of vision in his left eye. Neurological findings were normal except for the unilateral blindness and mild optic atrophy in the affected eye. Roentgenograms of the sella and general physical examination likewise revealed no abnormalities. In a letter to his doctor the unusual nature of the catastrophe was noted, and "Brain Tumor Suspect" was mentioned, together with the advisability of recheck. Some anomaly of the ophthalmic artery, possibly aneurysm, was hazarded as a specific diagnosis. This "long shot" guess struck the fancy of the referring doctor who told the patient that the condition was inoperable. The verdict was accepted and years later when vision started to deteriorate in the other eye, no doctor was consulted. Six years after the first neurosurgical examination he eventually reported to another neurosurgeon with a far advanced, hopeless suprasellar pituitary adenoma.

Still Under Observation. Nineteen of the "brain tumor suspect" cases are listed as "still under observation." These patients are all adults with continuing complaint of epilepsy. They have had pneumoencephalograms, and one or more equivocal electroencephalograms. When seizures are under control they report at intervals of 6 months to 1 year. They are encouraged to come back during the intervals if the pattern of seizures alters or if any other symptoms develop. The possibility of tumor is not suggested to the patients to ensure that they will report. Intelligent patients sense the problem, and do not ask difficult questions.

CONCLUSIONS

Within reason, and without creating unnecessary panic, more of these patients need to be impressed with the importance of follow-up. The neurosurgeon has been requested to rule out tumor. He can reasonably insist, in cooperation with other doctors concerned, that specific plans for follow up be established. When the neurosurgeon does not perform the follow-up himself, he should attempt to set the stage properly. This requires clear communication with another doctor who appreciates the problem, or with the patient himself.

Dr. Harvey Cushing[1] employed the term "brain tumor suspect" in a report to the American Neurological Association in 1923. Recognizing that the patients were sent to his clinic because some outstanding symptom suggested possible tumor, he admitted that often the best that he and his assistants could do was "temporarily to diagnose the case on a symptomatic basis." He further stated: "We have been deceived so often by discarding tumor in favor of another diagnosis that we incline toward this diagnosis until it can be disproved, rather than the reverse." Thirty-three years have passed. That still seems to be good advice.

REFERENCE

1. Cushing, H. Notes on a series of intracranial tumors and conditions simulating them. Tumor suspects; tumors unverified; tumors verified. *Arch. Neurol. Psychiat., Chicago,* 1923, *10:* 605–668.

EFFECTS OF HYPOTHERMIA ON LOCAL BLOOD FLOW AND METABOLISM DURING CEREBRAL ISCHEMIA AND HYPOXIA*

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THE recent use of hypothermia to prevent anoxia during temporary occlusion of cerebral blood vessels allows a more satisfactory approach to many neurosurgical procedures, particularly in cases of intracranial aneurysms, cerebrovascular malformations and vascular tumors.[2,3,9–11] It is possible that, with a better understanding of its mechanism, hypothermia may have wider therapeutic application in the treatment of cerebral ischemia, hypoxia, trauma and increased intracranial pressure.

We wish to report here polarographic changes in oxygen tension of cerebral cortex and brain stem resulting from temporary respiratory anoxia before and after hypothermia. In addition, clinical observations have been made which give information concerning the functional state and metabolism of the cerebral neurones during hypothermia. Observations have been made on 7 cats and 3 monkeys (*Macacus mulatta*). Some preliminary observations on human cerebral cortex are included.

METHODS

a) *Experimental Animals.* Concurrent records have been made of the local oxygen availability in several small areas of cerebral cortex and brain stem by the modification of the polarographic method described in earlier studies.[13–15] A silver-silver chloride anode is used in the form of a silver wire coated with silver chloride. The active electrode (cathode) consisted of finely tapered and exposed tips of 0.01-in. platinum wires insulated with Teflon. The exposed point is 1 mm. in length, tapering to a point. The principle of the method requires a potential of 0.6 V. supplied to the anode by a potentiometer. The platinum electrode is connected to the negative pole of the potentiometer through a resistance of 1.2 million ohms. On either side of this resistance, leads are taken to the input of a vacuum-tube micro-ammeter. The output of this instrument is recorded on bromide paper with a kymographic camera. Changes in cortical temperature are measured by a calibrated microglass thermistor bead used as a sensitive resistance thermometer.[13,14]

Concurrent records were made of the cortical temperature, rectal and axillary

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† With the technical assistance of Robert C. Struzziero.

temperatures, the cortical pH, electroencephalogram and steady potential, together with the blood pressure, electrocardiogram and respirations. In some experiments the intracranial pressure was also recorded with a strain gage screwed into a trephine hole in the skull. The technique of recording these parameters *in situ* has been described previously.[13,14]

In some experiments the corneal, pinna, tendon and pupillary light reflexes were tested at various temperatures. The cortical stimulation threshold was also measured before and after hypothermia, using a Grass stimulator model S4B.

The animals were anesthetized with Nembutal, 0.5 mg. per kg. of body weight, and, in several instances, chlorpromazine, 2 mg. per kg., was also given. Recordings were made in the steady state at normal body temperature (35°–37°C.). Observations were then made of the effect of brief occlusion of each carotid artery for measured periods of time. In some experiments the middle cerebral artery was occluded. Occlusion was produced by light traction on silk ligatures previously passed around these vessels. The effects of brief breathing of nitrogen and carbon monoxide were recorded, also the effects of breathing oxygen and 7 per cent CO_2 and oxygen mixtures.

The body temperature was then lowered by partially immersing the animal in an ice-water bath and the above observations were repeated for purposes of comparison at different body temperatures.

Measurements were also made of the diameter of cortical arteries and veins with a microscope at various temperatures, using techniques which will be described in a later communication.[14] In 5 animals the brains were immediately removed in the hypothermic state, fixed in 10 per cent formalin and stained with the Nissl and the benzidine methods.[5]

b) *Studies in Man.* In the neurosurgical operating room the principal observations noted in the cat and monkey have been confirmed in man. For example, polarographic records were made during the course of an operation for excision of an arteriovenous malformation of the frontoparietal cortex in a patient who had suffered from repeated episodes of subarachnoid and intracerebral bleeding. Premedication consisted of 50 mg. each of chlorpromazine, Phenergan and Demerol. Anesthesia was maintained with endotracheal administration of a mixture of oxygen, nitrous oxide and ether. The body temperature was lowered in the operating room with a refrigeration blanket. Axillary, cortical and rectal temperatures were recorded together with the blood pressure, electrocardiogram and electroencephalogram. The effects of occlusion of the common carotid artery on local availability of cortical oxygen and electroencephalogram were compared at temperatures of 37°C. and 29.8°C. The artery was occluded in the neck for periods of 50 sec. by means of a Blalock clamp.

In the operating room the polarograph anode and three platinum electrodes were mounted on a Grass cortical electrode holder.* The electrodes and electropolarograph were constructed along lines similar to those used in the animal experiments. Teflon insulation of the electrodes permitted them to be autoclaved. The micro-ammeter readings were recorded by hand on graph paper at 4-sec. intervals. An adjustable microglass thermistor bead was also mounted on the electrode holder so that measurements could be made of any small changes in cortical temperature.[13] Cortical electrograms were made with a Grass Electroencephalograph Model III-D.

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* Grass Instrument Company, Quincy, Massachusetts.

Related clinical, polarographic and pathological observations were made on 7 additional patients who were treated with hypothermia for varying periods of time. Three of these patients had thrombotic occlusion of one internal carotid artery, 1 had severe cerebral contusion and laceration, 1 had subarachnoid bleeding from an intracranial aneurysm and 2 had an intracerebral hemorrhage. Pathological examination of the brains at necropsy were made in 2 of these patients who died after 2 and 3 days of maintained hypothermia; 1 of the patients who died had a massive intracerebral hemorrhage and the other had massive infarction of one cerebral hemisphere consequent upon occlusion of one internal carotid artery.

RESULTS

a) EXPERIMENTAL ANIMALS

Hypothermia is more rapidly induced with the addition of chlorpromazine and pentobarbital (Nembutal) than with pentobarbital alone since shivering is abolished. In other respects the results are the same whether hypothermia is induced with or without chlorpromazine. Chlorpromazine enchances the sedative effects of pentobarbital. The temperature falls more rapidly in those portions of the body immersed in ice water. In experiments reported here, the lower limbs and abdomen were immersed in the ice bath. The rectal temperature decreased more rapidly than the axillary and cortical temperatures but the latter bore close correlation (Figs. 3, 4, 7 and 8). Conversely, when the animal is rewarmed by immersion in warm water the rectal temperature rises much more rapidly than the axillary and cortical temperatures (Fig. 4). The brain appears to cool homogeneously and the temperature of the brain stem does not vary significantly from that of the cortex during hypothermia. When the cortical temperature is decreased to 30°C. significant changes occur. The electroencephalogram decreases in frequency and progressive slowing occurs as the temperature is decreased further. This confirms the observations of a number of previous investigators.[1,2,3,7,9,10] Localized abnormality present in the electroencephalogram prior to hypothermia may still be recognized with temperatures as low as 25°C., and localized or generalized abnormality in the electroencephalogram will be seen if cerebral hypoxia eventually occurs. The present experiments in animals confirm that during hypothermia there are no electroencephalographic changes when the carotid artery is occluded for several minutes[2,9,10] and that the electroencephalogram may show no change for 6–8 min. of breathing 100 per cent nitrogen when the cortical temperature is 28°C. In general the lower the cortical temperature below 35°C., the greater the latency before ischemic or hypoxic changes appear in the electroencephalogram.

Blood Pressure. With progressive hypothermia there is a fall in arterial blood pressure. The fall in blood pressure is slight at 33°C. but marked at 30°C. or below.

Size of Vessel. Measurements of cortical arteries and veins with the micrometer microscope show a progressive reduction of the caliber of these

vessels beginning at 32°C. and becoming more marked at lower temperatures. The changes are most evident in arteries having a diameter approximating 200 mμ. The caliber of these vessels may be reduced by as much as 50 per cent at temperatures of 30°C. and below. Veins of similar caliber become reduced by about 25 per cent but active blood flow is still present. The capillary bed appears pale and poorly defined at 30°C. Histological examination of the vascular architecture of animals sacrificed at temperatures of 25°C. to 30°C. reveals a reduction of the red cell content of all cortical, subcortical and brain-stem vessels when compared with control sections of animals sacrificed at 37°C.

The intracranial pressure in the cat and monkey decreases by 3–10 mm. of water during the induction of hypothermia (Figs. 5 and 6). As the intracranial pressure is zero in the steady state this small negative pressure is considered to be significant. In the hypothermic state prolonged cerebral anoxia does not bring about an increase in the intracranial pressure (Fig. 6). The exposed brain after craniotomy at 29°–31°C. appears smaller than at 37°C. and has been exposed for 12 hours at these low temperatures without evidence of swelling.

Neuronal Excitability. Below 29°C. the animal makes little or no spontaneous movement even if the anesthesia is very light. When the animal is rewarmed, sluggish spontaneous movements begin at 30°C. and at 35°C. the animal is normally active.

The pupillary light reflex, the corneal, pinna and vibrissa reflexes become diminished at 27°–29°C. but are still obtainable (Figs. 3 and 8). Below 27°C. the pinna and vibrissa reflexes frequently disappear but the pupillary and corneal reflexes, although sluggish, are still present at 26°C. (Fig. 5). When the animal is rewarmed the reflexes promptly return to normal activity.

Threshold of Cortical Stimulation. The threshold parameters for cortical stimulation in the left frontal cortex of the cat ("X" in Fig. 8) which produced flexion movements of the right forepaw were 5 V., 60 c.p.sec. and 1 msec. at a rectal and axillary temperature of 37°C. This threshold remained unchanged at temperatures between 20° and 37°C. (Fig. 8).

Steady Potential. The cortico-cortical and cortico-subcortical steady potential (or D.C. potential) is unchanged when the body temperature is reduced from 37°C. to 25.5°C. (Figs. 5 and 6). However, prolonged anoxia or ischemia at low temperatures will produce a reversible shift of steady potential (Figs. 5B and 6). The threshold for change of steady potential with anoxia and ischemia is raised in a manner comparable to the threshold for electroencephalographic changes, i.e., the lower the temperature the greater the protection.

Respirations. Lowering the body temperature below 33°C. brings about a progressive slowing of respirations (Figs. 3, 4, 5, 6, 7 and 8). At cortical temperatures of 26.8°C. the chemoreceptor reflexes of the carotid body and the baroreceptor reflexes of the carotid sinus are preserved (Figs. 3, 4, 5 and 6). The hyperventilation brought about by hypoxia acting on the carotid

body is, however, significantly reduced. When the body temperature is lowered to 21°C., some delayed but prolonged respiratory stimulation may still be produced by anoxia (Fig. 8E). The sustained increase in depth and rate of respirations caused by breathing a mixture of 7 per cent CO_2 and oxygen at low body temperatures is striking (Fig. 3A).

As the body temperature is lowered there is an increasing degree of protection of the respiratory center from ischemic and anoxic anoxia. It has been shown previously[17] that, in the normothermic animal, 45–60 sec. of breathing 100 per cent nitrogen results in transient respiratory slowing with reversible anoxic damage to the respiratory center. Longer periods of breathing nitrogen result in respiratory arrest, gasping, and ataxic, pneumotaxic or periodic breathing. At body temperatures between 21° and 30°C. breathing of 100 per cent nitrogen can be tolerated for 5–10 min. with recovery (Figs. 6 and 8E, F). Such prolonged anoxia is invariably fatal in the normothermic cat or monkey.

Local Availability of Cerebral Oxygen, pH and Circulation. With the reduction of body temperature from 37° to 21°C., there does not appear to be a significant change in the availability of oxygen in the cerebral cortex or carotid arterial blood. The electrodes in the brain show a fall of $2\times10-8$ A. at 25°C., compared to readings at 35°C. This degree of fall is comparable to the change produced by cooling the electrodes through a similar range of temperature when placed in normal saline, for control purposes. The response of the electrodes to changes in partial pressure of the oxygen in the control saline solution is not changed.

Observations were made on the partial pressures of oxygen in different parts of the brain in order to study any arteriovenous changes. If the respirations are greatly slowed there may be a significant fall in the availability of oxygen in the cortical venous blood as measured by an electrode placed on such a vessel. This reduction, amounting to 20–40 per cent, is believed to represent an increased cortical arteriovenous oxygen difference, consequent upon decreased respiratory exchange.

In order to study arteriovenous changes further, three polarograph electrodes of equal size were calibrated in saline by passing nitrogen or oxygen through the solution at different temperatures and obtaining comparable changes in each. These three electrodes were then placed on a cortical intervascular space, on its artery of supply and on the vein draining the area. When records are made in this manner at 37°C., a highly reproducible sequence of events occurs when 100 per cent nitrogen is breathed instead of air (Fig. 1A). The arterial electrode records a reduction in the partial pressure of oxygen before a related reduction in the vein or tissue space, and the arterial gradient of fall is steeper than that of vein or tissue space. This is presumed to indicate that the partial pressure of oxygen in the arterial blood is reduced to a greater degree with breathing of 100 per cent nitrogen than in the vein or tissue space. The addition of 2 per cent carbon monoxide to the inspired air, however, does not significantly change the partial pressure of oxygen in the arterial blood but the carrying capacity

of oxygen is reduced by the formation of carbonmonoxyhemoglobin. The arterial partial pressure of oxygen is not greatly changed until the animal is terminal. The vein and tissue space thus show a reduction in availability of oxygen because the carrying capacity of arterial oxygen is insufficient for tissue demand, and cerebral ischemia, respiratory irregularity and a rise in blood pressure result (Fig. 1B). Breathing of oxygen produces a rapid increase in the partial pressure of the arterial oxygen and a slower increase in the tissue space and vein. The venous oxygen tension continues to rise

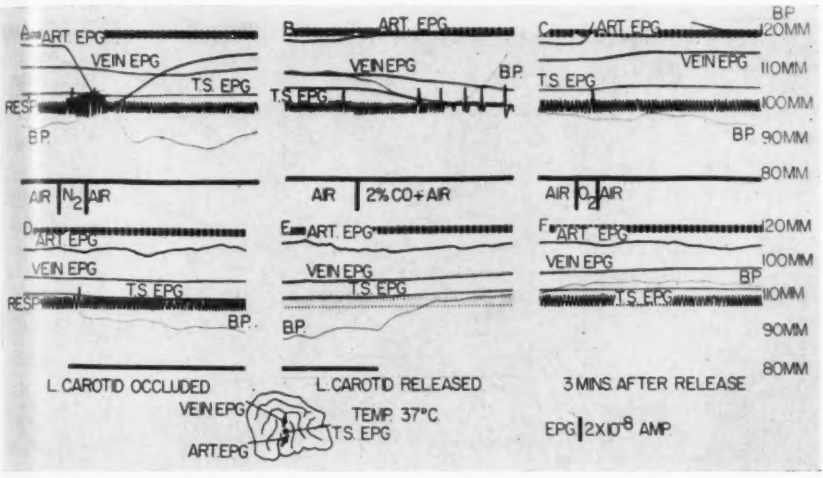

FIG. 1. Cat. Nembutal anesthesia. Six records from same experiment as in Fig. 2. To show effects of 100% nitrogen breathing, 2% carbon monoxide breathing and occlusion of left common carotid artery at a body temperature of 37°C. (see text). Oxygen electrodes placed on cortical artery (Art. EPG), vein (Vein EPG) and tissue space (T.S. EPG). EPG calibration at base of figure. Initial arterial EPG calibration = 25×10−8 A. Vein EPG = 17×10−8 A. Tissue space EPG = 8×10−8 A. Femoral blood pressure (B.P.) calibrated to right of C and F. Time marker at top of each record indicates 6-sec. intervals. Resp. = respirations. EPG = oxygen availability.

after the availability of the arterial oxygen is returning to the steady state, when air is resumed (Fig. 1C). These observations will be discussed in detail in another publication.[17]

Occlusion of the common carotid artery when the oxygen electrodes are recording from the opposite hemisphere, results in an irregular rise in the availability of arterial oxygen in the contralateral hemisphere which is attributed to an increase in the collateral blood flow.[15] The veins and tissue space do not show the irregular rise but a slower, smoother response (Fig. 1D). The irregular increase in the availability of arterial oxygen persists for 2–4 minutes after release of the left common carotid artery and then subsides. The vein and tissue space show a delayed but similar response (Fig. 1E, F). This is believed to be caused by reactive hyperemia. Occlusion of the common carotid artery supplying the same hemisphere from which the electrodes are recording results in a fluctuating reduction in the availability

of oxygen measured by the arterial electrode; this is followed by a parallel but less fluctuating pattern in the vein and tissue space (Fig. 2A). After prolonged occlusion a rhythmic rise occurs prior to release in the arterial electrode, which is followed later by similar changes in tissue space and vein (Fig. 2A). This phenomenon has been discussed in detail in another publication and the evidence indicates that it is the result of compensation by the cerebral collateral circulation.[13–15] From the observations reported here, the development of the collateral circulation and the reactive hyperemia conse-

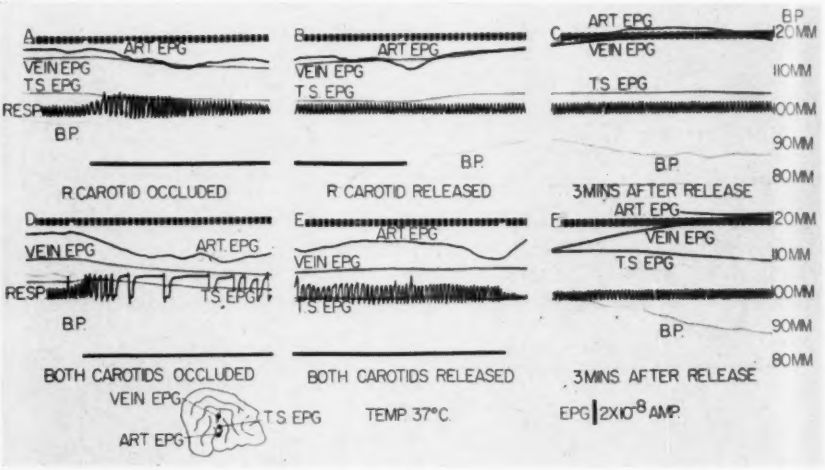

FIG. 2. Cat. Nembutal anesthesia. Six records from same experiment as in Fig. 1. To compare effects of occlusion of right common carotid artery (A,B,C) and both common carotid arteries (D,E,F) at a body temperature of 37°C. (see text). Oxygen electrodes placed on cortical artery (Art. EPG), vein (Vein EPG) and tissue space (T.S. EPG). EPG calibration at base of figure. Initial arterial EPG $=25\times10-8$ A. Vein EPG $=17\times10-8$ A. Tissue space EPG $=8\times10-8$ A. Femoral blood pressure (B.P.) is calibrated to right of C and F. Time marker at top of each record indicates 6-sec. intervals. Resp. = respirations. EPG = oxygen availability.

quent upon ischemia appear to be mediated by changes in the arterial blood supply. When the carotid is released a supernormal phase ensues, as shown in Fig. 2B, C. Occlusion of both carotid arteries with an associated fall in blood pressure produces a similar pattern except that the gradient and degree of cerebral hypoxia is greater and signs of cerebral anoxia ensue with pneumotaxic respiration (Fig. 2D). Release of both carotids results in a supernormal phase (Fig. 2E, F).

Modification of Anoxic and Ischemic Anoxia by Hypothermia. The modification of this series of events by hypothermia is illustrated in Fig. 3. In this experiment the arterial electrode was placed in the cerebral tissue space close to an artery. Fig. 3A records the effect of breathing nitrogen for 24 sec., Fig. 3B shows the effect of occlusion of the right common carotid artery and Fig. 3C the effect of breathing 2 per cent carbon monoxide for 30 sec. at a temperature of 37°C.

Figs. 3D, E, F and G were recorded for comparison when the cortical temperature had been lowered to 28–29.5°C. In Fig. 3D the reduction in availability of para-arterial, venous and tissue-space oxygen consequent upon breathing nitrogen for 24 sec. is not as severe as prior to hypothermia. The pattern of change in the tissue space is least affected while the arterial and venous gradient of fall is less steep and only 40–50 per cent of that seen in Fig. 3A. In Fig. 3E the decrease in availability of oxygen consequent upon

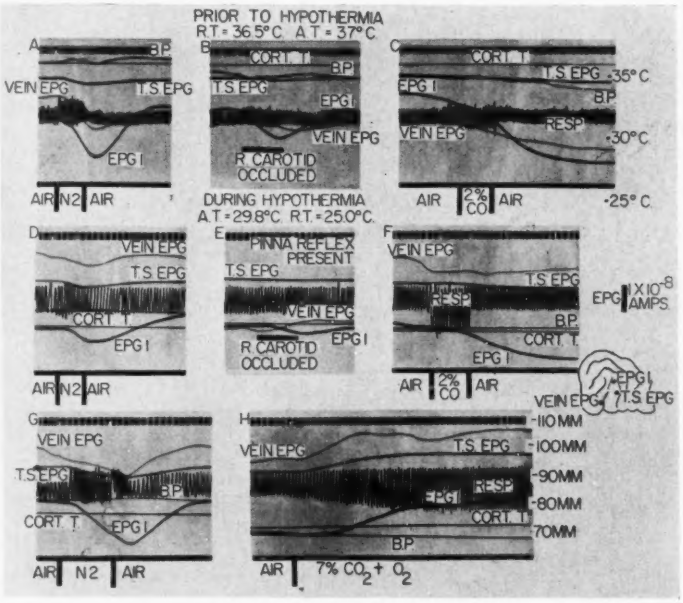

FIG. 3. Cat. Nembutal anesthesia. Eight records from same experiment as in Fig. 4. Rectal (R.T.) and axillary (A.T.) temperatures are recorded above each record. To show protective effects of hypothermia against 100% nitrogen, 2% carbon monoxide and vascular occlusion. H shows effect of breathing 7% CO_2 mixture during hypothermia. Blood pressure (B.P.) calibration is to right of H. Initial readings: Para-arterial EPG 1 = 20×10−8 A. Vein EPG = 19×10−8 A. Tissue space (T.S. EPG) 8×10−8 A. EPG calibration to right of record. Time marker indicates 6-sec. intervals. Resp. = respirations. EPG = oxygen availability.

occlusion of the right common carotid artery is reduced by 50 per cent or more.

At lower temperatures the degree of reduction in availability of oxygen in the cerebral cortex consequent upon occlusion of one or both carotid arteries is further lessened both in gradient and degree of fall (Fig. 8A, B, C, D). At 26.8°C. the reduction may be only 25 per cent of that at normothermic levels (Fig. 8B, D). The protective action of hypothermia in association with occlusion of the middle cerebral artery in the monkey is similar to that observed with carotid occlusion.

The modification by hypothermia of the effect of breathing 2 per cent

carbon monoxide is shown in Fig. 3C and F. In order to produce a comparable reduction in the availability of oxygen in the cortex during hypothermia at 28.5°C. (Fig. 3G) to that obtained with breathing nitrogen for 24 sec. at 37°C. (Fig. 3A) it was necessary to administer nitrogen for 48–72 sec. (Figs. 3G and 4C). Breathing a mixture of 7 per cent CO_2 and oxygen produced a marked and sustained increase in rate and depth of respiration and a marked rise in availability of cerebral oxygen (Fig. 3H). When the same animal was rewarmed to 32.5°C. or above, the protective effect of hypothermia against ischemic and anoxic anoxia was no longer remarkable (Fig. 4D, E, F). After rewarming, the pattern of change in the records caused by anoxic and ischemic anoxia was similar to that obtained at 37°C. (Fig. 3A, B, C).

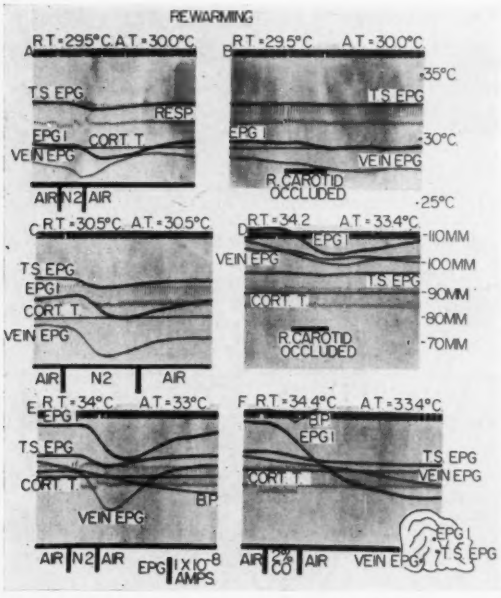

FIG. 4. Cat. Light Nembutal anesthesia. Six records continued from same experiment as in Fig. 3. Rectal (R.T.) and axillary (A.T.) temperatures are recorded above each record. To show decreasing protection of brain from ischemic and anoxic anoxia as brain is rewarmed. Blood pressure (B.P.) calibration to right of D, cortical temperature (Cort. T.) calibration to right of B. EPG calibration at bottom of record. Time marker indicates 6-sec. intervals. Resp.=respirations. EPG=oxygen availability.

Intracranial Pressure. Hypothermia produces a slight but significant reduction in intracranial pressure. The lower the temperature, in general, the greater is the reduction in pressure (Figs. 5 and 6). At low temperatures the intracranial pressure is affected by changes in venous and thoracic pressures. In Fig. 5A and B, for example, the rise in intracranial pressure consequent upon the hyperpnea of nitrogen breathing is similar at cortical temperatures of 34.2°C. and 26.8°C. When Cheyne-Stokes respiration is induced at a cortical temperature of 25.5°C. by prolonged breathing of nitrogen, fluctuations

in intrathoracic pressure are reflected in the intracranial pressure recording (Fig. 6).

Cerebral Blood Flow and Oxygen Transport. There is slight if any alteration in uptake of pulmonary oxygen or in blood flow from the lung to the brain, as measured by the techniques described here, until temperatures below 28°C. are reached (Fig. 5A, B). Below 25°C. a decrease in rate of effective oxygen transport to the brain may be demonstrated when equal

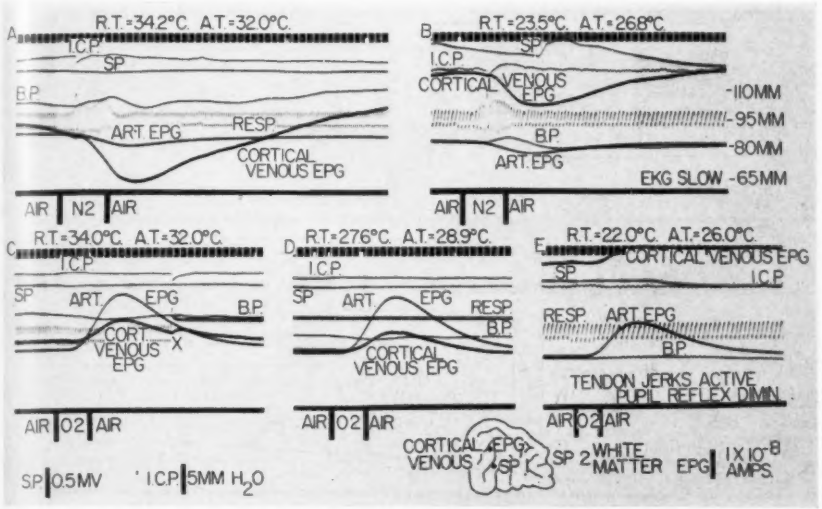

FIG. 5. Cat. Five records at different body temperatures from same experiment as in Fig. 6. Rectal (R.T.) and axillary (A.T.) temperatures are recorded above each record. Nembutal-chlorpromazine anesthesia. To show fall in blood pressure, reduction in intracranial pressure (I.C.P.), absence of injury potential (SP) and effects of brief nitrogen and oxygen breathing with progressive hypothermia. Nitrogen breathing produces a small SP shift in B. Art. EPG is in the wall of the artery. Cortical venous EPG (placed on a cortical vein) was moved up 2×10−8 A. between A and B. Initial carotid artery EPG reading=25×10−8 A.; cortical venous EPG=17×10−8 A. Blood pressure calibration to right of B. Time marker indicates 6-sec. intervals. At X pneumograph was displaced. Resp.=respirations. EPG =oxygen availability.

amounts of oxygen are breathed at 32°C. and 26°C. (Fig. 5C, D, E). This is caused, presumably, by slowed respiration and an increased circulation time. It should be noted, however, that the availability of cortical venous oxygen increases by the same amount and persists longer at high levels when oxygen is breathed at 26°C. than it does in the normothermic state. This is thought to represent a decreased arteriovenous oxygen difference when neuronal metabolism is reduced.

The gradient of reduction in availability of the carotid artery oxygen during hypothermia is not as steep during breathing of 100 per cent nitrogen as in the normothermic state (Fig. 6). This is apparently because the metabolism of oxygen of the entire body is decreased. This conclusion was sup-

ported further when calibrated electrodes for recording local availability of oxygen were placed in muscle, cerebrum and respiratory center. Breathing of oxygen produced a greater rise in availability of oxygen in muscle during hypothermia than was shown in comparable records in the warm state (Fig. 7A, C). Breathing of nitrogen during hypothermia demonstrated decreased utilization of oxygen in muscle, brain stem and cortex.

pH. The pH of cerebral cortex varies closely with the respiratory ex-

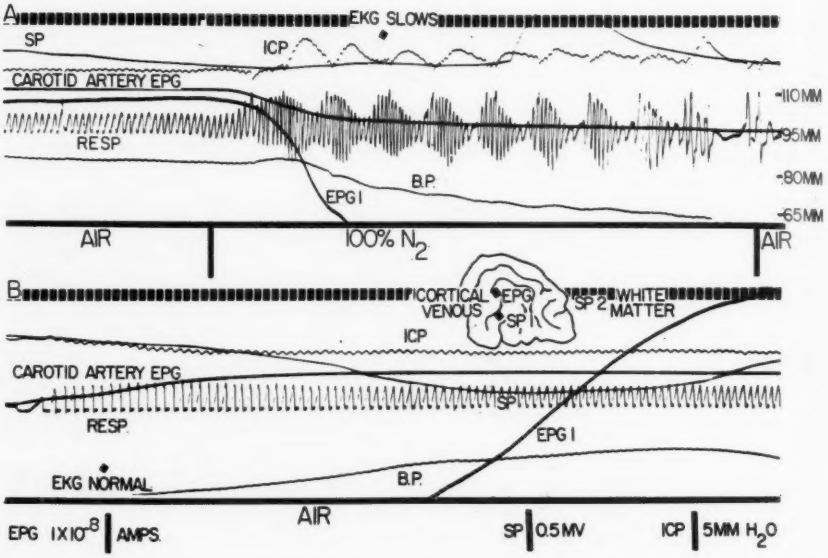

FIG. 6. Cat. Axillary temperature 25.5°C., rectal temperature 21°C. Same experiment as in Fig. 5. B is continuous from A. Nembutal-chlorpromazine anesthesia. To show protection of respiratory center from anoxic damage with 100% nitrogen breathing for 6 min. Transient Cheyne-Stokes respiration resulted. EPG shown on brain diagram on cortical vein. SP = Steady potential between cortex and subcortical white matter. ICP = Intracranial pressure. 48 sec. of nitrogen breathing produced rapid increase in cerebral arteriovenous oxygen difference. EKG changes are noted on record. Blood pressure calibration to right of A. Initial carotid artery EPG reading = 25×10−8 A., cortical venous EPG reading = 15×10−8 A. Time marker indicates 6-sec. intervals. Resp. = respirations. EPG = oxygen availability. This illustration has been used in another publication on a different subject.[17]

change during hypothermia. If a small reduction in respiratory rate occurs, the pH shows a corresponding increase in acidity (Fig. 8A, B, C). If the respirations are markedly slowed at lower temperatures the cortex shows a greater fall in pH (Fig. 8D). Severe respiratory slowing (as with anemia of the respiratory center in Fig. 8E) brings about a cortical acidity by as much as 0.5 pH units. An increase of the respiratory rate results in a slow return of the cortical pH to the steady state (Fig. 8E).

In the normothermic preparation, cerebral ischemia results in localized acidity (Fig. 8B). During hypothermia below 33°C., a comparable degree

of ischemia does not result in cortical acidity. The development of cortical acidity consequent upon prolonged breathing of nitrogen[13,14,17] is also markedly diminished during hypothermia (Fig. 8E).

When a 7 per cent mixture of CO_2 and oxygen is breathed during hypothermia the availability of cortical oxygen is increased considerably more than when 100 per cent oxygen is breathed. This increase is greater than seen in the normothermic state and it is believed to represent a dilatation

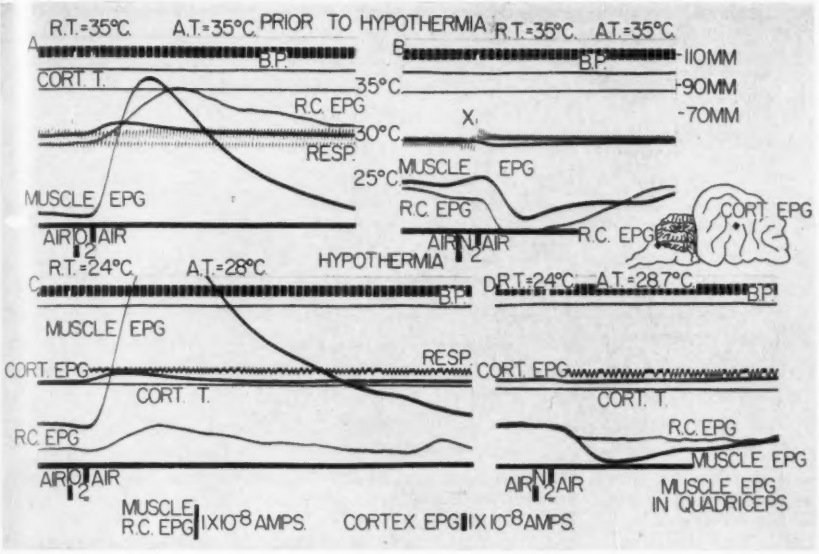

FIG. 7. Cat. Four records from same experiment. Rectal (R.T.) and axillary (A.T.) temperatures are recorded above each record. Light Nembutal-chlorpromazine anesthesia. To compare effects of brief oxygen and 100% nitrogen breathing before and after hypothermia with oxygen electrodes placed in cortex (Cort. EPG) and respiratory center (R.C. EPG). In A and B the unmarked dark trace superimposed on the respiratory record is the cortical EPG (Cort. EPG). Cort. T. = cortical temperature, calibrated to the right of A. EPG in muscle and respiratory center have different calibration than cortex EPG, as shown at base of B. Pneumograph displaced at X. Time marker indicates 6-sec. intervals. EPG = oxygen availability.

of constricted vessels during hypothermia as well as increased respiratory exchange.

During the induction of hypothermia the rate of reduction of cortical temperature is more rapid between 30°C. and 25°C. than between 35°C. and 30°C. At 30°C. any rhythmic fluctuations in availability of cortical oxygen and temperature cease. When the animal is rewarmed the temperature of the brain increases more rapidly between 30°C. and 35°C. than between 25°C. and 30°C. and small rhythmic fluctuations in temperature and availability of oxygen reappear. This cessation of vasomotion correlates with the vasoconstriction seen with the microscope.

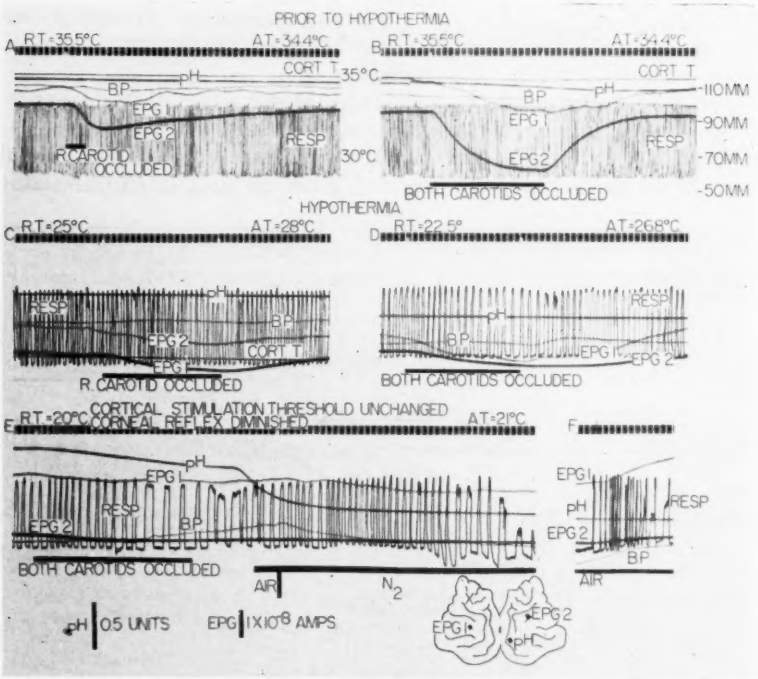

FIG. 8. Cat. Six records from same experiment. Rectal (R.T.) and axillary (A.T.) temperatures are recorded above the record. Nembutal anesthesia. To compare effects of unilateral and bilateral carotid occlusion before and after hypothermia and 100% nitrogen breathing for 10 min. at a body temperature of 21°C. F is 6 min. after E. Blood pressure (B.P.) calibration to right of B. Cortical temperature (Cort. T.) calibration to right of A. Positions of cortical polarograph electrodes (EPG 1 and EPG 2) and pH electrode (pH) shown on brain diagram. EPG and pH calibration at base of record. Initial reading of EPG 1=19.5×10−8 A., EPG 2=11×10−8 A. Time marker indicates 6-sec. intervals. Resp.=respirations. EPG=oxygen availability.

b) RESULTS IN MAN

The induction of hypothermia in man by use of the refrigeration blanket and intramuscular premedication with Demerol, Phenergan and chlorpromazine results in a rapid lowering of the body temperature without shivering. As would be expected, those areas of the body in direct contact with the blanket cool more rapidly than the cerebral cortex. The electroencephalographic changes with progressive hypothermia in man have been described by others,[2,9,10] and consist in general of a progressive reduction in frequency as the temperature is lowered below 30–32°C.

We have noted that focal abnormality present in the electroencephalogram at 37°C. can still be recognized at low body temperatures. In one patient a continuously discharging spike focus was unchanged in the electroencephalogram at 29.8°C. We have also confirmed that during hypothermia

there are no electroencephalographic changes (as recorded from the exposed cortex) when the carotid artery is occluded for several minutes.[2]

Blood Pressure and Respirations. As the body temperature is lowered there is a progressive fall in arterial blood pressure.[9,10,12,18,19] At 29°C. the blood pressure becomes difficult to obtain by the auscultatory method, but by palpation the systolic blood pressure is usually 90 mm. Hg. Respirations become slow and machine-like in quality.

Size of Vessels. The systemic veins become collapsed at temperatures between 29 and 33°C. and venipuncture is difficult. Ophthalmoscopic examination at 30°C. reveals pallor of the optic discs and reduction in the caliber of retinal arteries and veins. The cortical vessels appear less prominent at this temperature and there is little bleeding on section of the cortex.

Neuronal Excitability. Observations made on patients free of sedation during hypothermia between 29° and 31°C. have not, in our limited experience, shown any variance from those of other observers.[20] Below a body temperature of 31°C. the patient lies quietly, making little movement. Patients are drowsy and stuporous during treatment but they are not comatose unless because of preceding brain injury, sedation or the body temperature falls below 27°C. Some postural movements are made, and withdrawal of the extremities may be elicited with painful stimulation. The eyes may move and gaze at the examiner and minimal vocalization may be made. The pupillary light reflex and corneal responses are sluggish but present between 28° and 30°C. It is still possible at this temperature to recognize such signs as a hemiparesis, spasticity and asymmetry of the reflexes.

Intracranial Pressure. During hypothermia the exposed brain appears slightly diminished in size. Other observers have remarked on this appearance of the brain.[2,11] Two patients in the present series in whom brain swelling was demonstrated at operation in the normothermic state (consequent upon massive cerebral infarction in one and cerebral hemorrhage in the other) showed little if any evidence of brain swelling or herniation at necropsy subsequent to 48–72 hours of treatment with hypothermia.

In another patient* the cerebrospinal fluid, venous and blood pressures were continuously recorded with strain gages and an ink-writing polygraph. At 37°C. the cerebrospinal fluid pressure was 125 cm. of water and became reduced to 100 cm. of water at 33°C. However, at this temperature positive pressure breathing or respiratory hypercapnea promptly increased the cerebrospinal fluid pressure, and an increase in venous pressure resulted in a corresponding increase of cerebrospinal pressure.

Cortical Blood Flow and Availability of Oxygen. Observations made at operation on 2 patients in whom it was necessary to clamp the carotid artery gave satisfactory confirmation of the foregoing polarographic data in experimental animals. For example, in the patient whose record is illustrated in Fig. 9, a right-sided craniotomy was performed for excision of a small

* Dr. Walter Wegner performed the surgery in this case and kindly cooperated in the recorded observations.

arteriovenous vascular malformation, and the right common carotid artery was occluded with a Blalock clamp for 50 sec. The cortical temperature and availability of oxygen in the distribution of supply of the carotid artery were recorded during the time the vessel was occluded. The artery was again occluded for 50 sec. after hypothermia had been induced and the cortical temperature was 29.0°C. The rate of reduction of availability of oxygen was slower and the degree of fall was reduced by 75 per cent of that seen at 37°C.

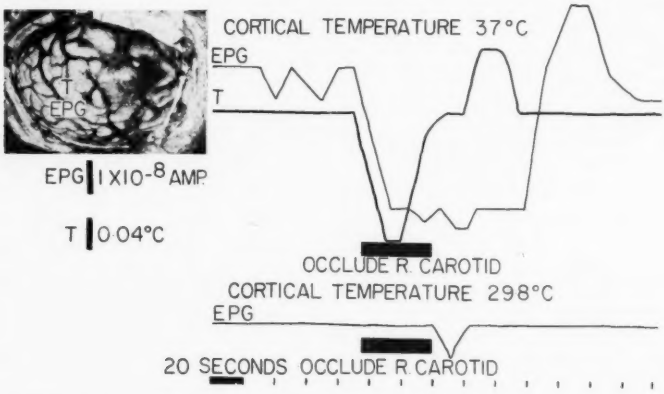

FIG. 9. Records of cortical oxygen availability (EPG) and temperature (T) in a patient who underwent excision of an arteriovenous malformation during hypothermia. Compare the fall in oxygen availability produced by clamping the right carotid artery with that obtained by the same procedure at 29.8°C. Operative photograph at top of figure shows position of electrodes in parietal region. Calibration of EPG and T are shown at left, and time intervals of 20 sec. are marked at base of record. Base-line sway of EPG prior to occlusion was caused by movement artifact in operating room. B.P. at 37°C. was 120/60 and at 29.8°C. was 90/60. EKG was regular throughout operation.

(Fig. 9). Records made in another patient showed a similar small, delayed reduction in availability of cortical oxygen in the Sylvian region when the ipsilateral common carotid artery was occluded with a Selverstone clamp at 33°C.

DISCUSSION

Hypothermia may be defined as the lowering of body temperature in a normally warm-blooded (normothermic) species and is accompanied by consistent physiological changes, some of which provide advantages in neurological and neurosurgical therapy. The over-all reduction of body metabolism[17] is of particular significance with regard to the central nervous system because of the high metabolic rate of cerebral tissue.

Data presented here indicate that there is a more or less linear reduction in consumption of cerebral oxygen as the temperature is reduced below 33°C. This reduction is dependent on a decreased rate of cerebral metabolism. It does not appear to be caused by the shift in the oxygen dissociation curve towards a lower partial pressure of oxygen or an inability of the brain to extract oxygen from the blood at lowered temperatures.[9]

There is also a decreased cerebral blood flow accompanied by a generalized reduction in the calibre of the cerebral vessels. This is probably secondary to the decreased cardiac output and mean blood pressure but may also be mediated in part by decreased cerebral metabolic factors acting as local vasodilators.

Cerebral metabolism is dependent on oxygen and glucose. While stores of glucose are available in brain there is no oxygen reserve.[8,13] In the normothermic state the brain can withstand ischemia or anoxia for 8–12 sec. before symptoms and electroencephalographic abnormalities appear.[16] During hypothermia the reduction of cerebral metabolism affords significant protection of the entire central nervous system against anoxic or ischemic anoxia. In addition, the reduction of cerebral blood flow renders surgery relatively bloodless, and decreases cerebral volume and intracranial pressure. The reduction of intracranial pressure together with protection of the brain from anoxia and its consequent changes in the permeability of the cerebral vessels[4,12] tends to prevent edema of the brain.

The experimental studies reported here would indicate that cerebral metabolism is significantly reduced at 31°C. or below, and that ischemia and hypoxemia can be circumvented for prolonged periods of time at such low temperatures. Above this temperature the decreased metabolism is present, but the degree of protection is less prolonged or predictable. Optimum body temperature for protection from severe ischemia or hypoxemia would appear to be between 28°C. and 31°C., since below 27°C. cardiac irregularities are liable to occur[9,10,18,19] and respiratory slowing may significantly alter the body pH.

This proposed optimum therapeutic temperature range correlates well with the work of Gänshirt *et al.*,[6] who measured cerebral survival and revival times after brief but total cerebral ischemia at different body temperatures. These authors found that the survival time was progressively increased with reduction in body temperature. Their results indicate that the prolonged survival time became significant below 30°C. The recovery latency, however, was shortest at 30°C. but below this temperature it was progressively prolonged. From their data they concluded that the optimum protection of brain against ischemic damage is between 27°C. and 30°C., if both survival and rapidity of functional recovery are considered.

The protective effects of hypothermia in cerebral ischemia and anoxia suggest that in addition to its usefulness in neurosurgery, it might also be useful in such conditions as carbon monoxide poisoning, increased intracranial pressure and in cerebral contusion and laceration. In cerebral contusion and laceration reduced cerebral blood flow has been shown to cause local cerebral metabolic disturbances and consequent cerebral edema.[12] Hypothermia tends to protect the brain against these effects of impaired blood flow and consequent brain swelling. Others have reported the therapeutic usefulness of hypothermia in such conditions.[11] Our own limited clinical experience leads us to believe that wider therapeutic evaluation is indicated.

Nature of Hypothermic Neuronal Paralysis. The results reported here indi-

cate that hypothermia produces a varying degree of reversible metabolic neuronal paralysis which may be readily controlled by alteration of the body temperature. As the temperature of the brain is lowered, neuronal metabolism and function progressively decrease.

Polarographic measurements fail to show a significant reduction of tissue oxygen available to the cell. Thus cold appears to produce a progressive histotoxic paralysis of the metabolic enzymes of the nerve cells of the central nervous system. The absence of the production of acid metabolites following ischemia and hypoxia also indicates reduced neuronal metabolism. The absence of a shift in the steady potential and of change in the threshold of cortical stimulation indicate that the cell membrane is still functionally intact. The electroencephalogram indicates a progressive reduction in neuronal activity.

The clinical pattern of the loss of neuronal function in man caused by hypothermia suggests that the neuraxis is paralyzed in a descending manner. The cortex is affected early, followed by diminution in the reflexes of the upper brain stem. Respirations are slowed at lower body temperatures but the spinal reflexes are relatively spared.

Evaluation of Recovery During Hypothermia. The question of when hypothermic treatment should be stopped in each patient is a difficult question to answer satisfactorily since the disorder for which treatment is instituted has usually resulted in a serious neurological deficit.

We have found that a limited evaluation of a patient's neurological status can still be made when the body temperature is reduced to 29°C.-30°C. At such temperatures the fundi can still be well visualized and a withdrawal response to painful stimulation occurs. In one patient with infarction of most of the right hemisphere it was possible to demonstrate a hemiplegia, increased reflexes on the paralyzed side and an abnormal plantar response.

Serial electroencephalograms and measurements of cerebrospinal fluid pressure may also aid in the decision to terminate the treatment with hypothermia.

SUMMARY

1. Studies of tissue oxygen tension, pH, blood flow, electroencephalogram, steady potential, reflexes, respirations and blood pressure have been made in experimental animals before and after hypothermia and the principal observations have been confirmed in man in the neurosurgical operating room.

2. The effects of cerebral ischemia and hypoxia have been evaluated before and after hypothermia.

3. Hypothermia results in a decreased cerebral blood flow, cerebral vasoconstriction and a progressive decrease in cerebral metabolic rate as the body temperature is lowered. There is no significant reduction of tissue oxygen available to the nerve cell.

4. Hypothermia produces a varying degree of reversible, metabolic

neuronal paralysis which may be controlled by alteration of the body temperature.

5. On the basis of physiological studies, hypothermia has therapeutic potentialities in preventing or lessening cerebral ischemia and anoxia as well as being of value in the treatment of increased intracranial pressure.

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CASE REPORTS

AN EXCEPTIONAL CASE OF INJURY OF THE FEMORAL NERVE

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A recent article by Clare[2] on femoral nerve repair reminded me of the following case which I observed in November 1950. It was quite similar to the one in which operation was performed by Scoville.[6]

CASE REPORT

The patient was a young woman, 21 years of age, who had been operated upon elsewhere for appendicitis on July 7, 1950. Soon after the operation she experienced serious difficulties in the movements of her right leg.

Examination. On Nov. 5, 1950, she was seen in consultation with a neurologist (Dr. I. Ruggeri). The principal findings, apart from a scar in the right iliac fossa near Poupart's ligament, were: atrophy of the right thigh, which measured 4.5 cm. less than the left in circumference. Active flexion of the thigh was possible, but with diminished force; extension of the leg was impossible; external rotation of the leg was limited; and the patellar reflex was absent. Anesthesia was present on the anteromedial surface of the thigh and the inner side of leg and foot. There was faradic inexcitability of the quadriceps femoris and sartorius; these muscles showed reaction of degeneration. Evidently the right femoral nerve had somehow been injured in the course of the previous operation.

Operation. On Nov. 7, 1950 the nerve was exposed in both the iliac and inguinal fossae, through a T-shaped cut along the old scar and a lower perpendicular incision. Not only was there a complete section of the femoral trunk above Poupart's ligament, but there was a noticeable displacement of both neuromatous stumps: the distal one cranially and medially, the proximal one in the retroperitoneal scar tissue. The two ends were freed from the surrounding scar, and the neuromas were resected, leaving proximally the well fasciculated end of the crural nerve trunk, and distally the section of two terminal branches. The gap between them measured about 5 cm. Suture, with fine silk, was possible after ample mobilization of the stumps, and flexion of the thigh. This position was fixed with a plaster spica, which was removed after 3 weeks.

Postoperative Course.

March 10, 1951 (4 months after operation): No change was evident.

Jan. 19, 1952 (14 months postoperative): Atrophy of the thigh was considerably diminished; active extension of the leg was possible. In the supine position the patient was able to lift the thigh from the bed, with the leg extended. Rotation of the leg appeared normal. The patient was able to walk without support, but found some difficulty in going upstairs. The anesthetic zone was less wide. Electrical responses of the quadriceps and sartorius were unchanged. The patellar reflex was absent.

Oct. 11, 1952 (about 2 years after operation): The circumference of the right thigh was only slightly less than that of the left. The force with which the leg could be extended was nearly normal, though some difficulty in going up and down, or in walking on uneven ground, persisted. The patellar reflex was still absent. There was moderate hypoesthesia (and sometimes hyperpathia) over a limited strip on the medial aspect of thigh and leg. There was no response to faradic stimulation of the quadriceps, and there was moderate reaction of degeneration.

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Recently (over 5½ years after the nerve suture) we have written to the patient concerning her present condition, but failed to obtain any answer.

DISCUSSION

The infrequency of traumatic injuries to the femoral nerve (when compared to other peripheral nerves) might be ascribed to more than one cause: (a) the nerve is quite short, measuring only a few centimeters from its origin to its branching at the level of Poupart's ligament; (b) it is well protected on its dorsal side, and is fairly deep on the ventral aspect; (c) its topographic relations with the iliac vessels, the intestine and the bladder may render difficult the clinical appreciation of its injuries, when they happen to be concomitant with injuries of one or more of these other structures. In fact, the patient may die in a very short time, and the acute and menacing symptoms are apt to obscure the neurological defects. Incidentally the latter might explain, at least partially, the considerable difference in frequency of injuries of the lumbosacral and the brachial plexuses.

It is rather difficult to understand how the femoral nerve came to be injured in the course of an appendectomy, when one considers that the nerve is not only retroperitoneal, but is also protected by the iliac fascia, and the nerve itself is fairly thick. Possibly there were very extensive adhesions.

Until I read about Scoville's case[6] I thought that mine was unique. The best way to cope with the disability caused by an interruption of the femoral nerve seems to be suture of the divided ends, either primary or secondary. The primary operation has many advantages: it is easier, and regeneration of the nerve is more prompt. But an operation done after some time has elapsed also should not prove too difficult, at least judging from the reports of Clare[2] and Scoville,[6] and the present case.

In the Italian literature I found a case of femoral nerve injury operated upon by Scaglietti[5] (1942). The nerve had been injured at the groin by a shell fragment, which had also fractured the neck of the femur. At operation, 4 months after injury, the nerve was found embedded in dense scar tissue just at the level of the nerve's branching. Suture was not considered feasible, and neurolysis was performed, without any improvement. As in Scaglietti's case, suture may prove difficult when the interruption is at the level of the terminal branching of the nerve, especially if this is in the shape of a *patte d'oie*, instead of the division into two principal branches.[3]

Judging from the few cases published, it seems that suture of a divided femoral nerve may be followed by gratifying and fairly prompt results, which compare favorably with those obtained after suture of the radial nerve. As a matter of fact the function of these two nerves is very similar, and fairly simple, while reactions are executed by long and robust muscles. As is known from physiological and clinical grounds, such conditions favor recovery.[1]

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PANTOPAQUE INTRAVASATION (EMBOLIZATION) DURING MYELOGRAPHY

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Hinkel[4] first noted and described the phenomenon of intravasation of Pantopaque during myelography in 1945. His was the unique experience of fluoroscopically watching the contrast medium disappearing spontaneously from the spinal canal. "As the patient coughed, I saw a marked and bizarre change in the pantopaque column. It appeared to extend in all directions like a star-burst. The original subarachnoid oil column shrank rapidly, and branching, slender finger-like columns of oil were seen extending to the right, the left, caudad and cephalad from it. Within fifteen seconds no oil could be seen in the subarachnoid space and a broad oil column was seen forming to the right of the lumbar spine. It was at once realized that the oil had entered the venous system."

Four years later in 1949 Fullenlove[2] similarly witnessed the rapid disappearance of the contrast medium: "The pantopaque was seen to leave the spinal canal through the venous plexus in the area, and within three minutes the greater part was gone."

Steinbach and Hill[6] in 1951 reported a case in which 7.5 ml. of Pantopaque was left in the spinal canal when efforts to remove it were discontinued because of gross bleeding at the site of puncture. Subsequently intrathoracic distress developed and roentgenograms of the chest revealed the presence of "multiple small, fine, reticular densities . . . " in both lungs, interpreted as Pantopaque emboli. In the subsequent discussion, it is inferred that all of the contrast medium had disappeared from the spinal canal. A similar case[5] has been seen at the same institution since publication of the original paper; the details of the later experience are not as yet available.

More recently, Ginsburg and Skorneck[3] reported another instance of embolization in the lung visualized roentgenographically, following intravasation.

We believe that intravasation of Pantopaque during myelography is more common than the paucity of reported cases would seem to indicate.

CASE REPORT

A 47-year-old white man was admitted to the hospital on July 6, 1955, complaining of low-back pain with radiation down the posterior aspect of the right leg, numbness about the rectum, and loss of sexual power. He gave a history of having had two low-back operations within 3 days in 1941 for pain in the back and leg. Following the operations, right foot-drop was present and the pain persisted essentially unchanged. In October, 1954, there was spontaneous development of numbness about the rectum, impotence, and difficulty in initiating micturition. The above symptoms persisted without progression or remission.

Examination. There was marked weakness of dorsiflexion and plantar flexion of the right foot with atrophy of the calf and anterior tibial muscle groups. The right Achilles reflex was absent. Slight saddle hypesthesia and hypalgesia were present and there was more pronounced sensory loss over the anterolateral aspect of the right leg below the knee, extending over the dorsum of the foot. Straight leg raising was not limited and the Naffziger test was negative.

A lumbar puncture done at the L5 interspace showed normal dynamics, and cerebrospinal

fluid studies revealed no cells, a very faint trace of globulin and a slightly elevated protein of 69 mg. per 100 ml.

Roentgenograms of the lumbar spine revealed a transitional 1st sacral vertebra and evidence of a previous laminectomy with posterior fusion of L4 to S1.

Myelography. It was learned from the previous surgeon that a Thorotrast myelogram had preceded the operations in 1941. The contrast medium was reported to have been completely retrieved at the end of the procedure and none was demonstrable on the above-described films.

On July 7, 1955, lumbar myelography was performed. The introduction of the needle was atraumatic. A few milliliters of clear fluid were withdrawn and 9 ml. of Pantopaque were injected with the patient on his left side. He was then turned to a prone position and tilted head-down to move the contrast medium into the upper lumbar region. This area appeared to be normal and an anteroposterior spot film was taken. The column of oil was then returned to the lower lumbar area where a defect appeared fluoroscopically at the 4th lumbar interspace on the left, below which a pronounced narrowing of the sac was noted. Anteroposterior and oblique spot films were made. At this point the patient complained of "a tickle in my chest," and an irritative cough developed, but otherwise he seemed to be tolerating the examination well. When the patient was tilted to the upright position, it was noted by fluoroscopy that the amount of contrast medium had greatly decreased and the remainder was progressively disappearing. Successive films were taken rapidly to record this phenomenon until only approximately ½ ml. of Pantopaque remained. The spinal needle was withdrawn and a roentgenogram of the chest was made.

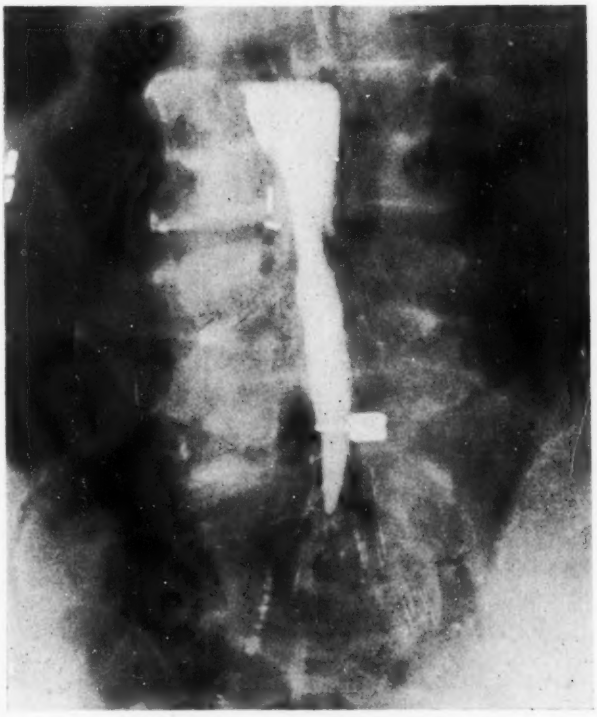

FIG. 1. Column of Pantopaque as it appeared when loss of volume was first recognized under fluoroscopy.

Course. The fundi were inspected in the event that small emboli might have filtered through the lung barriers and have reached the retinal vessels, but these examinations were negative. The patient continued to complain of mild tickling in the chest for several hours thereafter, but during this period the coughing subsided and no abnormal auscultatory signs were found. His temperature rose to 100.6°F. in the afternoons of the next 2 days—aside from this there were no subsequent signs or symptoms referable to the unusual episode.

When the films were reviewed in chronological order, successively smaller amounts of Pantopaque were demonstrated until the meniscus reached the level of the tip of the spinal needle where the shrinkage of the column ceased. A lateral roentgenogram clearly incriminated the forwardly displaced needle as the *modus operandi* for the escape of the opaque medium into the anterior internal venous plexus, and in all films, multilinear rivulets of medium were visualized streaming away from the spinal canal along the distribution of the lateral sacral and pelvic veins.

Roentgenograms of the chest taken at the time of the myelogram, 3 hours later, and periodically thereafter, were negative for emboli. A general roentgenological survey of the body done the following day was unremarkable except for films of the skull, in which numerous faint linear streakings suggested an intracranial venous distribution of contrast medium.

A program of conservative management of the presenting symptoms was initiated but this proved ineffective.

Operation. On July 20 a lumbar laminectomy was performed. Dense arachnoid and dural thickening and adhesions were found involving the cauda equina and emerging nerve roots of

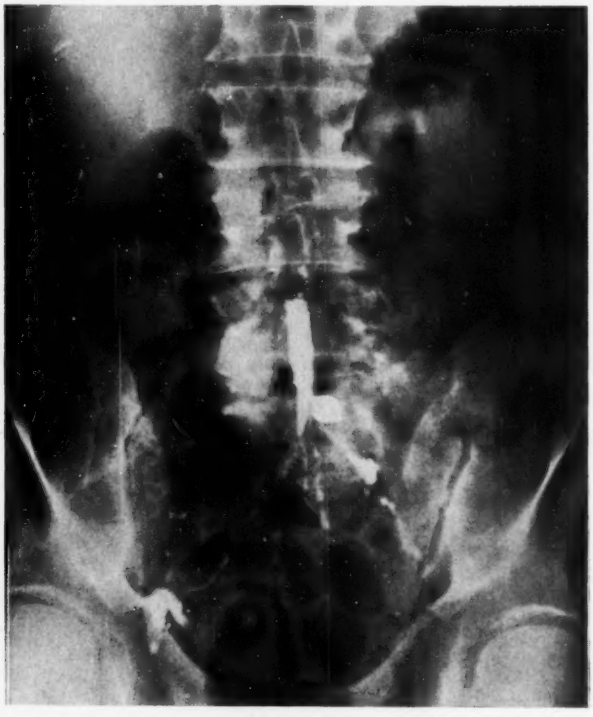

FIG. 2. Film made seconds after that shown in Fig. 1, demonstrating venous pathways of evacuation.

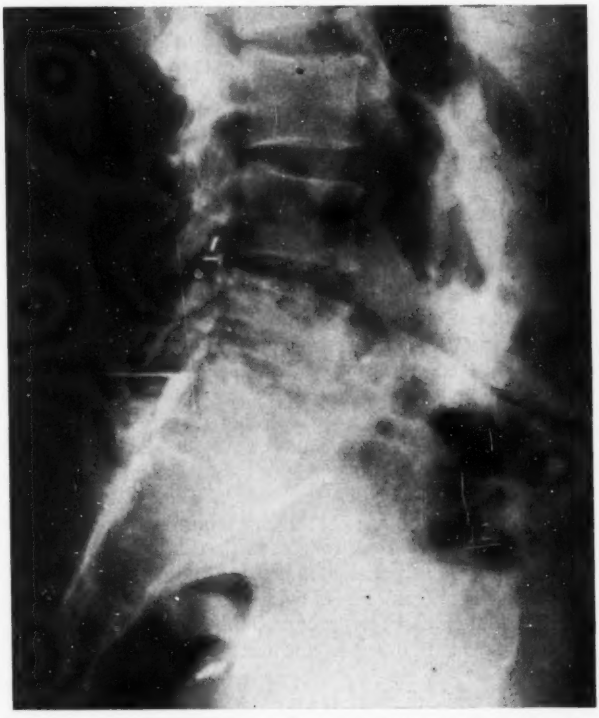

FIG. 3. Intravasation almost completed at level of spinal needle, illustrating the escape of contrast medium into the anterior internal venous plexus.

the lower lumbar and sacral spine. No effort was made to decompress or dissect out these incarcerated structures.

Course. Recovery from operation was uneventful and the patient was discharged essentially unimproved 22 days after admission.

DISCUSSION

Previous authors have described and demonstrated the venous pathways of intravasated Pantopaque as it escaped along the intervertebral veins to enter the lumbar and lateral sacral veins, eventually to collect in the inferior vena cava in accordance with our present knowledge of normal venous drainage from the lower spinal canal. Ginsburg and Skorneck[3] first presented roentgenological evidence revealing the actual passage of contrast medium into the venous channels, which in their case were the basivertebral veins. Fig. 3 is offered as evidence that in our case the Pantopaque passed from the subarachnoid space into the anterior epidural venous plexus along the forwardly displaced venipuncturing spinal needle.

Figs. 1 to 3 record the progressive dissemination of the opaque material which occurred in a matter of seconds.

Roentgenograms of the skull taken the day after myelography demonstrate numerous faint linear streakings suggesting that the material is in the veins rather

than in the subarachnoid spaces. It is postulated that this might represent a cephalad migration of the contrast medium along intraspinal venous pathways as advocated by Batson.[1] Continuous coughing may have effected rapid changes in intrathecal and venous pressures resulting in a cephalad surge of the dye along the network of venous plexuses, with ultimate ascension into the intracranial venous system. It is not clear why residual contrast medium could be visualized roentgenographically 24 hours later. No intracranial symptoms were elicited and, unfortunately, no subsequent roentgenograms of the skull were taken, so this supposition remains unsubstantiated. We are unable to present roentgen confirmation of Pantopaque embolization in the lungs.

CONCLUSIONS

Although venous intravasation of contrast media from the subarachnoid space during myelography has been described on only 6 occasions, it is likely that the actual incidence may be greater. The epidural space is occupied by a rich network of intercommunicating venous plexuses, and it has been well established that pressure within these veins is considerably less than that within the spinal fluid sac under normal circumstances. The evacuation of the contents of the intrathecal space into the venous system has been remarkably demonstrated roentgenographically by several investigators. It is reasonable to suppose that this is a not infrequent occurrence during the routine postmyelographic removal of contrast medium, as these efforts are often associated with variable amounts of trauma and obvious distress to the patients. The experience may be attended by immediate symptomatology, a delayed reaction, or no clinical evidence of abnormality. The potential for serious sequelae is unknown as recorded experience is hardly sufficient for significant conclusions in this respect. Symptoms and clinical manifestations were transitory in all published cases.

In those instances in which there is an apparent discrepancy between amounts of medium injected and withdrawn, or when an irritative cough, mild distress of the chest, and associated febrile reaction attend or follow myelography, especially in the presence of a bloody tap, intravasation is suggested as a reasonable explanation.

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TERATOMA IN REGION OF THE PINEAL BODY

REPORT OF A CASE*

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True teratomas in or about the pineal body are relatively rare. Only 28 such tumors were reported up to 1940.[11] In Cushing's series of 868 proven intracranial tumors, 4 or 0.5 per cent were teratomas.[5] Despite their rarity, they remain of great interest in that removal is rarely successful, delineation from other pineal tumors is difficult, and their cells of origin are obscure.

This case report illustrates the clinical and anatomical findings associated with a teratoma of the pineal body. It is of unusual interest for the following reasons: its large size; the strikingly short duration of symptoms; and the interesting problem posed as to how the lateral ventricular fluid drained with the 3rd ventricle obstructed by tumor.

CASE HISTORY

An 18-year-old airman was first seen by his medical officer in November 1954 because of loss of appetite of 4 months' duration. There had been no loss of weight. He was seen again in the early part of January 1955 because of pallor; the patient, however stated he felt well and his hemoglobin was 15 gm. per cent. On Feb. 9, 1955, he was admitted to an Air Force Dispensary with the history of having had severe bilateral frontal headaches for 2 weeks and intermittent vomiting for 4 weeks. The day before his admission he had been sitting on a stool drinking a soft drink when he suddenly felt his eyes "go bad" and he fell backwards. He recovered within a very short time but was somewhat dizzy on postural change. Diplopia on left lateral gaze had been present for 1 month prior to admission. He was then transferred to a civilian hospital where he was studied on the neurosurgical service.

Examination upon admission there revealed him to be pale, lethargic, and undernourished. The neck was not stiff and auscultation and percussion of the skull were normal. The gait and station were not tested. Findings on examination of the cranial nerves were as follows: I. Not tested. II. Fields were full to confrontation but there was slight haziness of the margins of the discs bilaterally. There were no hemorrhages or exudate and the arteriovenous relationship was 1 to 3. III, IV, VI. Pupils—the left measured 4 mm., the right 3.8 mm. There was no reaction to light bilaterally but reaction on accommodation was prompt bilaterally. There was diplopia on extreme lateral gaze. There was inability to elevate the eyes above horizontal and convergence was absent. V. Motor and sensory examination revealed no deficit. VII. There was no asymmetry on rest or with voluntary motion. VIII. Hearing was normal bilaterally. IX, X. He swallowed well and the palate elevated in the midline. The gag reflex was present, active and symmetrical. XI. The sternocleidomastoid and trapezius muscles were normal. XII. The tongue upon protrusion remained in the midline.

Motor examination revealed a slight tendency to wavering in all extremities, more particularly the left arm; there was no definite ataxia; there was increased muscle tone bilaterally, more marked on the left; and there was generalized hyperreflexia, also more marked on the left. The tests for dysdiadochokinesia were done fairly well bilaterally but slightly less well on the left. The left plantar response was extensor and the right was equivocal. Sensations to pin prick and position sense were normal.

* The opinions expressed in this paper are those of the authors and do not necessarily reflect those of the Bureau of Medicine and Surgery of the U. S. Navy.

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An electroencephalogram revealed a relatively centrally located lesion which was more on the right. Lumbar puncture revealed an initial pressure that fluctuated between 270 and 210 mm. of spinal fluid. The spinal fluid was clear but very slightly xanthochromic with 20 red cells, 36 lymphocytes and a protein of 270 mg. per cent. The blood hemoglobin was 12.5 gm. per cent; red cell count was 4.08 million, hematocrit 40, and white cell count was 5100 with a normal differential. Urine was normal. The blood urea nitrogen was 13 mg. per cent, total serum protein 6.7 gm. per cent, sodium1 53 mEq./l., potassium 4.0 mEq./l., chlorides 113 mEq./l. Roentgenograms of the skull revealed a collection of small calcific densities in the midline, somewhat inferior to the usual expected position of the pineal body. The radiologic diagnosis was that this probably represented a pineal tumor.

Because the patient was a service personnel he was transferred to the nearest military neurosurgical center on Feb. 17, 1955.

Examination. On admission the patient was slow of speech but oriented as to time, place and person. Neurological findings were essentially the same as previously recorded with the addition of a constant gross tremor of the left upper extremity which could be controlled by placing his hand behind his head. There was little change in his condition over the next 3 days. A radioactive isotope scan revealed a right-sided cerebral tumor with a projected location above the pinna of the ear.

Bilateral occipital trephinations were performed and the intraventricular pressure was measured on the left side. The pressure was found to be negligible, and the total protein was

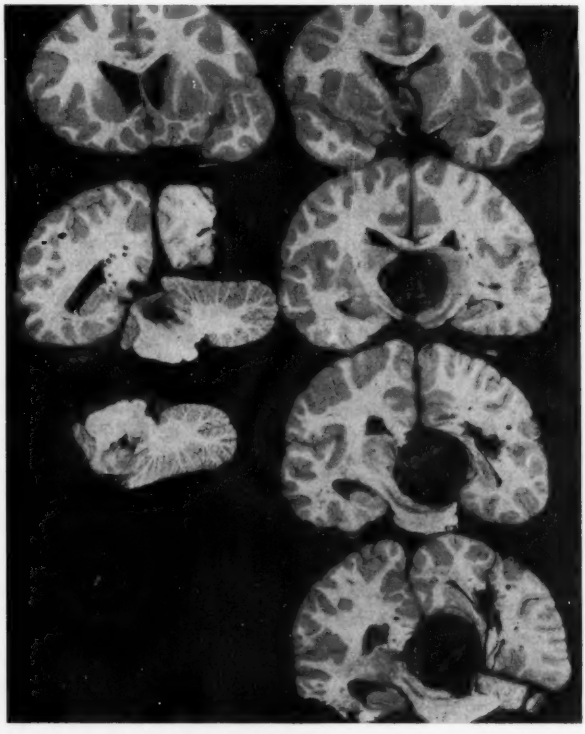

FIG. 1. Multiple coronal sections of the brain show the tumor extending from the anterior commissure (top right) to the 4th ventricle (bottom left).

80 mg. per cent. No air was inserted into the ventricle. An attempt was made to tap the right lateral ventricle but in doing so a cyst was encountered with the release of 5 cc. of very xanthochromic fluid. In view of the localization on the electroencephalogram, the radioactive scan, and the finding of the cyst on the right, it was felt that a ventriculogram was not necessary.

Operation. A right parieto-occipital craniotomy was performed and an extensive tumor was seen on the medial aspect of the right cerebrum near the splenium of the corpus callosum that extended past the midline. The tumor was encapsulated and brownish in color, with many small cysts which contained viscous brownish fluid. The content of the tumor could not be removed with a sucker because of its tenacity and the capsule could not be separated from the surrounding tissue with ease. Because of the extent of the tumor the operation had to be terminated.

Course. The patient's postoperative condition was very poor. He was deeply comatose,

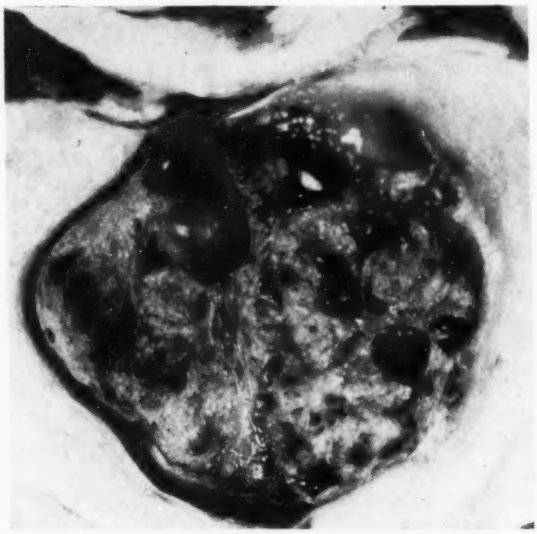

FIG. 2. Cross section of the tumor (section is second from the top right in Fig. 1) showing gross cysts with islands of gray tissue between. Compression of adjacent structures is also shown.

had Cheyne-Stokes respirations, and was in decerebrate rigidity. Three days following operation dye was inserted into the left lateral ventricle but it was not recovered in the lumbar spinal fluid. The patient's condition gradually deteriorated and he expired on Mar. 9, 1955.

Autopsy. Gross Examination. The craniotomy incision was healed with only small amounts of residual subgaleal fibrin. The bone flap was well anchored by silk sutures. Approximately 30 cc. of partially organized blood clot were present in the epidural space, and 20 cc. of xanthochromic fluid lay in the defect of the right occipital lobe. The major venous sinuses were patent and the falx and tentorium were intact.

The brain weighed 1450 gm. and showed moderate flattening of the gyri, early coning of the cerebellar tonsils, and moderate creasing of the uncinate gyri. A large surgical defect in the right parieto-occipital area extended through the posterior horn of the lateral ventricle to expose a lobulated, smoothly contoured mass in the region normally occupied by the splenium of the corpus callosum. The mass extended well to the left of the midline. Needle tracts were noted in both occipital lobes. After fixation in 10 per cent formalin, coronal sections were made (Fig. 1).

There was moderate hydrocephalus, best seen in the left lateral ventricle. A fusiform mass filling and obliterating the 3rd ventricle measured 6.5 cm. in length and 4.0 cm. in diameter. The tumor tapered to 1 to 1.2 cm. at the ends. On section, the tumor had a varied appearance, containing multiple cysts filled with greenish mucinous material, tough gray trabeculae with a gritty texture, and gray-white islands exhibiting small hemorrhages (Fig. 2). A smooth gray fibrous capsule measured 1 to 2 mm. at most places of contact with the ventricular wall. The anterior end of the tumor was nonadherent and rested on the anterior commissure, greatly dilating the supraoptic recess. In its midportion the tumor greatly distended the 3rd ventricle and compressed the periventricular structures. The optic chiasm was compressed from above and the optic tracts were spread apart by the bulging floor of the 3rd ventricle. The massa intermedia was not identified. The compressed thalami showed softening about the margins of contact with the tumor. With gradually decreasing diameter, the posterior extent of the tumor presented in the 4th ventricle, with elevation and thinning of the anterior medullary velum. The lamina quadrigemina was not identifiable as such, since only a thin translucent sheet of neurofibrillar tissue covered the tumor in the region of the aqueduct. The tegmentum of the midbrain and anterior pons showed compression and softening for a depth of 2 to 3 mm. There was indistinct delineation of tumor and neural tissue in the left anterior pontine tegmentum. The substantia nigra was flattened. The splenium of the corpus callosum was destroyed. The region of the pineal recess and posterior commissure was greatly distorted by encapsulated adherent tumor tissue. The pineal body could not be identified grossly or microscopically. The pituitary body was removed with some difficulty, being adherent to the sella turcica.

Microscopic Examination. Sections of tumor tissue from many areas showed a teratoma with large expanses of neural elements in neuroepithelial arrangement. Often, condensates of mesenchymal stroma contained osteoid tissue. Pulmonary elements were represented by primitive alveolar formation with ducts lined by respiratory mucosa leading from them. Hyaline cartilage and smooth muscle cells were in the walls of the ducts. Islands of squamous epithelium were present and some showed keratin granules. Much of the tumor was composed of undifferentiated mesenchymal tissue with some focal hemorrhages in it (Fig. 3).

Sections from the posterior part of the pituitary gland, including the infundibulum, showed complete replacement by numerous lymphocytes, often in aggregates. Numerous

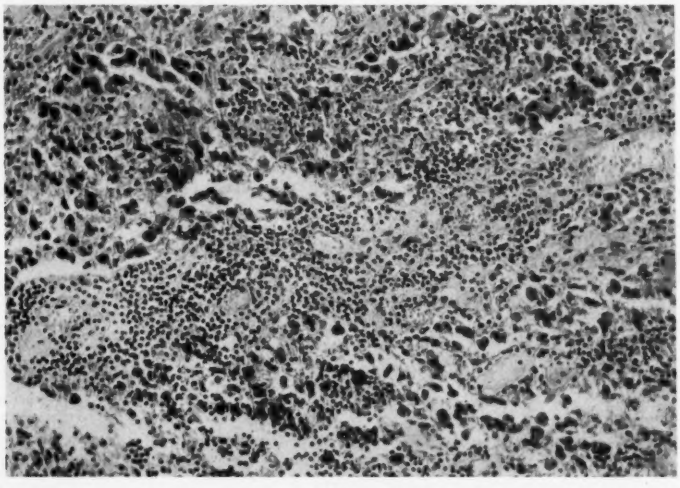

FIG. 3. Microscopic section of the infundibulum showing embryonal cells with lymphocytic infiltration. (Hematoxylin and eosin, ×125)

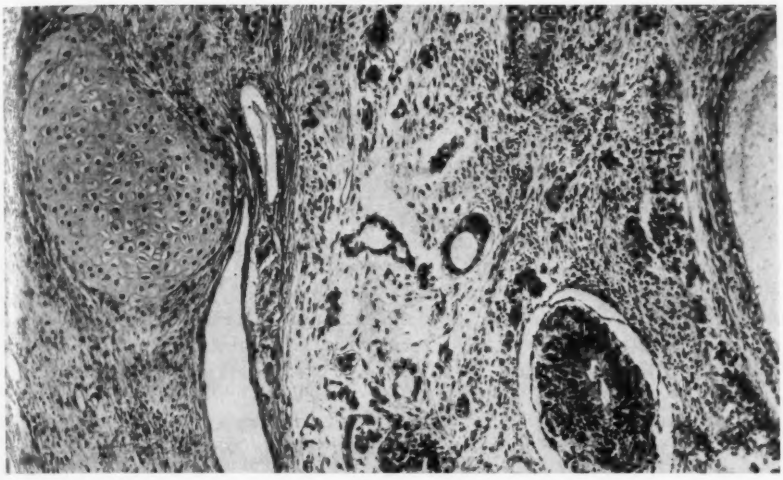

FIG. 4. Microscopic section of island of gray tissue in the tumor showing cartilage, cysts lined by mucus-producing cells, neuroepithelial clusters and mesenchymal stroma. (Hematoxylin and eosin, X65)

large polyhedral cells with hyperchromatic nuclei lay singly and in noncohesive cords (Fig. 4). These did not extend into the anterior lobe. Sections from the optic chiasm showed infiltration of the large polyhedral cells between bundles of fibers in the medial optic tracts. There was concomitant extensive perivascular lymphocytic infiltration. In no other area, including many sections from the region of the pineal body, were cells of this type found.

Sections of the thalami showed extensive periventricular compression with loss of neurons, oligodendroglia, and replacement by lipoid-filled macrophages. The body of the corpus callosum and the fornix were necrotic.

Sections from the medulla, cerebellum and left cerebral hemisphere showed neuronal reactions without degeneration. The walls of the right occipital surgical defect showed reparative changes with inflammatory reaction, hemosiderin and macrophages.

The right lung weighed 550 gm. and the left 250 gm. Both showed small quantities of edema and microscopic foci of bronchopneumonia. The heart, and mediastinal and abdominal viscera were normal. Multiple jejunal intussusceptions were easily reduced. Other organs, including the testes, were normal both grossly and microscopically.

DISCUSSION

This 18-year-old male died approximately 2 months after the onset of symptoms caused by a teratoma in the pineal region. The early neurological symptoms of headache and vomiting were probably caused by obstruction of the 3rd ventricle and aqueduct which resulted in moderate hydrocephalic dilatation of the lateral ventricles.

The duration of aqueductal obstruction is difficult to estimate. Symptoms of acute hydrocephalus began 2 months before death. The moderate degree of hydrocephalus found at autopsy would be consistent with this duration. It is difficult to conceive of flow of ventricular fluid around the tumor in the months or years preceding symptoms and equally difficult to assume the tumor grew so rapidly in the last few months that only then did it obstruct the 3rd ventricle and aqueduct. Fluid

could have escaped around the tumor through the defect in the corpus callosum or fluid production may have been suppressed. An intermittently patent foramen in the choroid plexus in the temporal horns of the dilated lateral ventricles may have existed. The walls of the 3rd ventricle were intact. Unfortunately none of these possible explanations can be proven.

The localizing ophthalmological signs were: Inability to elevate the eyes above horizontal; diplopia on left lateral gaze; absence of convergence; absence of reaction to light with preservation of reaction on accommodation; and pupillary inequality. These signs resulted from compressive destruction of the lamina quadrigemina and tegmental nuclei by the tumor and closely parallel those described in other cases of teratoma of the pineal body.[1–4,8,13]

The diagnosis of teratoma can be suspected from the roentgen-ray findings of abnormal calcific deposits in the region of the pineal body, as in this case, and confirmed if these calcifications take the form of teeth. A ventriculogram will localize obstruction of the 3rd ventricle, but in the present case this procedure was not deemed necessary.

The nomenclature for primary tumors of the brain composed of nonneurogenic tissues has led to confusion. A definition of a teratoma as "A true tumor or neoplasm composed of multiple tissues foreign to the part in which it arises" seems inconclusive.[12] Another definition requires derivatives of all three germ layers to be present.[11] As a result of nonconformity to a single definition, a wide variety of tumors have been included and the incidence of true teratoma is difficult to obtain.[6] The tumor described here satisfied both definitions and contained all three germ layers; to our knowledge it is the largest such tumor in the pineal region reported in the literature.

In many of the reported cases of teratoma in the pineal region, as in the present case, the pineal gland was not found because of apparent destruction by the tumor. This suggests these tumors may often arise in the pineal body.[7,10] In 1 reported case there were pineal cells and corpora arenacea in one zone of the teratoma.[3] In another case reported as one of pineal teratoma there was an intact uninvolved pineal body at the time of surgical removal of the tumor.[8] These examples illustrate the difficulty in citing the actual site of origin of teratomas arising in the pineal region.

The source of teratomas in terms of their cells of origin remains elusive. It has been suggested that they arise from totipotent cells in the mature pineal body.[1] It was noted that the embryonic 3rd ventricle gives rise to many structures including the pallium, the optic vesicles, the infundibulum, the postinfundibular recess, the choroid plexus, paraphysis, pineal body, and the subcommissural organ. This multipotential *Anlage* was then considered an appropriate source for teratomas.[8] Cohnheim's inclusion theory would explain these tumors as maturation of blastomeric cells included in the midline fusions during organogenesis. In support of this is the young age of the patient when the tumor becomes manifest.[11] There is little doubt that the patient described here had his teratoma for a long period of time. It may have been present at birth or before. Colossal teratomas in the 3rd ventricle have been described in the newborn.[6,7,11]

The relationship of pinealoma to teratoma has been discussed and the identity of ectopic pinealomas with atypical teratomas has been suggested.[9,10] In the present case, the tumor cells in the infundibulum and optic chiasm probably represent embryonic elements or pinealomatous differentiation of the teratoma, and in that respect only it mimicked a so-called ectopic pinealoma.

No explanation is offered for the high incidence of this tumor in the male, whereas teratomas elsewhere in the body affect females slightly more often. The most frequent site of teratomas in the male is the testis, and the second most frequent is in the region of the pineal gland.[12]

Surgical removal was attempted here but because of the extent of the tumor the effort had to be abandoned. The localized nature and relative benignity of teratomas, as illustrated by their great size without extensive infiltration, should make them amenable to surgical extirpation. In no case of teratoma found in the literature have extracranial metastases been reported. However, their position in the brain makes any surgical undertaking hazardous. Reports of successful removal are encouraging but survival rates after removal are not.[2,4,8]

Hormonal studies were not done in this case but there was no history or evidence of macrogenitosomia praecox. This syndrome has been reported with teratoma of the pineal body.[3] If, as has been suggested, the presence of embryonal tissue induces a "pseudo-pregnancy state" in prepubertal males, resulting in macrogenitosomia praecox, this postpubertal patient may have had elevation in hormone titres.[1] Since only a very small proportion of the tumor was composed of embryonal cells this elevation would have been inconspicuous.

SUMMARY

A case of a large teratoma in the region of the pineal body is reported in which operative intervention was unsuccessful. A discussion of the size, source and origin of the tumor is presented with reference to pertinent literature.

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INVASION OF THE SPINAL CORD BY MALIGNANT SCHWANNOMA

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The spinal cord is subject to a variety of lesions that come under the classification of tumors. These may be primary tumors that originate within the spinal cord, or arise from implantation of tumor cells that are transplanted by the circulating cerebrospinal fluid, a situation not uncommon with medulloblastoma, but apparently occurring less frequently with other brain tumors. In addition, the spinal cord may be compromised by vascular malformations, hemangiomas, intramedullary cysts, and extradural lesions, such as metastatic tumors, abscesses, extradural cysts, intervertebral discs, and granulomatous lesions. Direct invasion of the spinal cord by tumor spreading by way of the peripheral nerves is a most unusual and relatively rare situation.

CASE REPORT

V.L., a 50-year-old male, was examined on Mar. 19, 1953. He complained of pain in the right side of the neck, right upper chest and shoulder, and in the right phantom arm. In 1944 an inflamed, dark mole near the right elbow had been cauterized. Three months later subcutaneous nodules appeared at the same site. During the next 6 years local recurrent tumor nodules in the subcutaneous tissues were excised on six different occasions. The successive recurrences progressed higher and higher on the right arm and were little affected by repeated courses of roentgen-ray therapy. Pathological diagnosis up to 1950 was recurrent fibrosarcoma. Dr. Arthur Purdy Stout believed the tumor was a recurrent leiomyosarcoma of the skin or subcutaneous tissue, although malignant melanoma could not be excluded.

By 1952 a tumor mass had appeared in the right axilla. Exploration revealed that the tumor had invaded and surrounded the brachial plexus; consequently the entire right upper extremity, including the shoulder girdle, was amputated. Following this operation a right Horner's syndrome developed and the patient experienced intermittent pain in the right side of the neck, right upper chest, shoulder and in the right phantom arm. The pain was aggravated by turning of the head to right or left. The phantom pain felt as if an ice pick were being driven through the back of his hand, or as if his fingers were being stretched or caught in a vise. On occasions he experienced a burning sensation which radiated from the right phantom elbow into the hand.

Examination. A mass was present in the right supraclavicular region. There were extensive surgical scars in the region of the right axilla. Positive neurological findings were a right Horner's syndrome, and anesthesia to pin prick over the right anterior aspect of the chest to the level of the nipple line. Pressure in the right supraclavicular region produced pain. Roentgenogram of the chest showed only minimal thickening of the pleura at the right apex.

Course. The patient's pain was well controlled with Empirin and codeine, and surgical measures for its relief did not seem justifiable.

In May, 1953 the patient was reexamined because weakness of the right leg had developed, followed by weakness in the left leg, associated with difficulty in emptying his bladder and controlling bowel movements. The pain in the neck, chest and phantom arm was unchanged.

The superficial abdominal and epigastric reflexes were now absent. Deep reflexes were moderately active and equal throughout, and there were no definite pathologic toe signs or

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ankle clonus. There was moderate weakness of both lower extremities, more marked on the right. Position sense and vibratory sensibility were slightly impaired in the right lower extremity. Light touch was preserved everywhere. There was hypesthesia to temperature and pain below the 1st dorsal cord segment on the left, and anesthesia, as before, was present to the level of the nipple line in the right anterior chest wall. The spinous processes of the 7th cervical and 1st dorsal vertebrae were tender.

A Pantopaque study on May 26, 1953 showed a nearly complete block opposite the 7th cervical vertebra, only a small amount of oil being able to pass on the left side. The spinal fluid was clear and colorless, and contained a total protein of 25 mg. per cent and 6 white blood cells.

Operation. On May 27, 1953, laminectomy from the 3rd cervical to the 2nd dorsal vertebra revealed no evidence of extradural tumor. The right laminal arch of the 1st dorsal vertebra was softer than normal. At the level between the 6th and 7th cervical vertebrae the spinal cord was greatly swollen. The dentate ligaments were cut bilaterally. The 7th and 8th cervical roots on the right side were swollen to about four times their normal size. The 6th and 7th intervertebral foramina on the right were widened and tumor could be seen growing into the substance of the spinal cord through the dural sleeve. The right 7th and 8th cervical roots were cut in the hope of giving the patient some relief from his pain.

Pathological Study. Sections of the nerve roots showed tumor. On comparison with material from previous operations, it was found to be generally identical in structure. Despite the numerous recurrences, the pattern was that of a fairly mature spindle-cell sarcoma in most places. The tumor was within the nerve sheath, and suggested sarcoma of nerve-sheath origin (malignant schwannoma). Hence it seemed that the principal spread of the lesion had been along nerve trunks. The morphologic structure of the tumor was compatible with such an origin. The tumor had presumably arisen as a peripheral nerve neurofibrosarcoma in the skin or subcutaneous tissue and had shown a predilection to spread along nerve trunks, a well known method of extension for tumors of this group.

The tumor was composed of fairly uniform spindle cells forming many interlacing bundles. The individual cells showed fairly distinct cell borders, pale and faintly fibrillary cytoplasm, and elongated, evenly stained nuclei. Nucleoli were not prominent in many cells, while other cells showed large, evenly stained nucleoli. Mitotic figures were infrequent. A mild leukocytic infiltration was present.

Postoperative Course. The patient tolerated the operation reasonably well, but increasing paresis and finally paraplegia confined him to bed, with inability to void. During the next 5

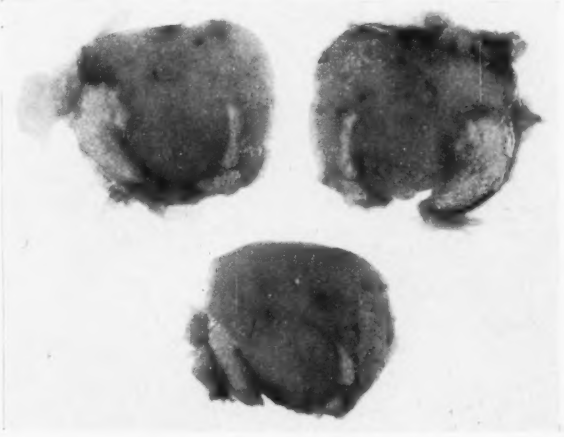

FIG. 1. Gross appearance of transverse section of lower cevical cord. (×1½)

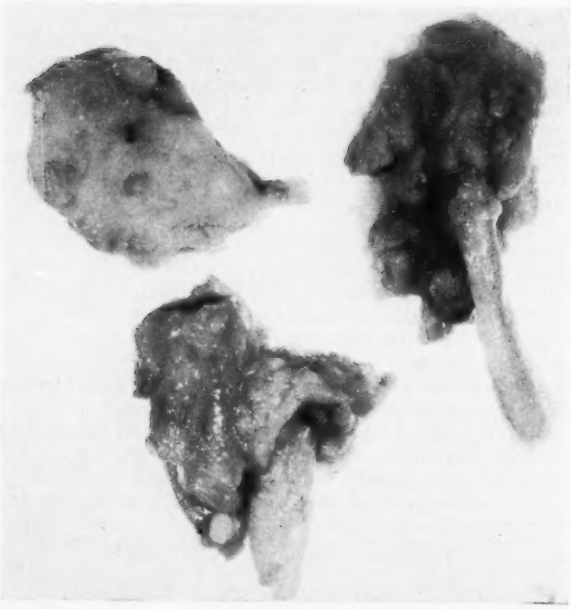

FIG. 2. Gross appearance of nerve trunks entering tumor mass in brachial plexus. ($\times 1\frac{1}{2}$)

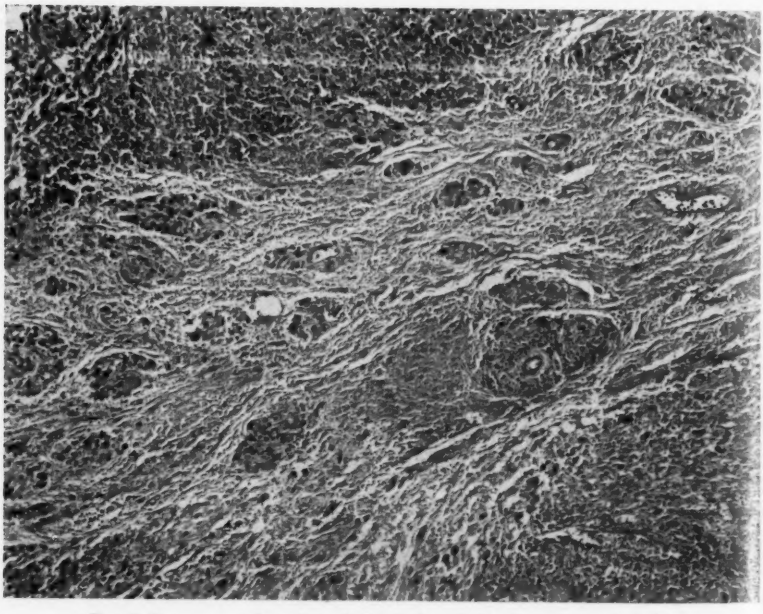

FIG. 3. Low-power view of cervical spinal cord showing masses of tumor cells within degenerated cord. ($\times 75$)

months he experienced increasingly severe pain in the right side of the neck and right shoulder, finally requiring almost constant opiate medication for relief. The left arm became gradually weaker and more atrophic. Increasing respiratory distress developed, and he expired Oct. 11, 1953, 9 years after the onset of an inflamed, dark mole near the right elbow.

Autopsy. Spinal Cord. The lower cervical canal was completely filled with a roughly cylindrical mass of gray tumor measuring 2 cm. in diameter and extending for 8 cm. The tumor was not adherent to the dura mater except as it surrounded the nerve roots. On transverse section near the center was a gray mass which was of the size and shape of the spinal cord. Lateral to this were two white, roughly crescent-shaped masses of soft and friable tissue, presumably nervous, which almost met. On one side, gray tumor was found peripherally and laterally, so that one crescent-shaped white mass was completely embedded within tumor (Fig. 1). At one end of the mass the tumor was reduced in amount and the spinal cord was intact and round, although extremely soft and friable. *Brachial Plexus.* In the right brachial plexus a mass of pearly gray, firm tumor tissue, measuring 5.0 cm., overlay the mid portion of the right clavicle and extended beneath the clavicle and into the neck along the normal course of the brachial plexus. Near the vertebral column, nerve trunks were visualized on the external surface of this tumor (Fig. 2). On cross section they were pearly gray and incorporated into the tumor. Within the large mass of tumor in this vicinity were yellow zones of necrosis and also visible nerve trunks embedded deep within the tumor. *Lungs.* Two discrete tumor metastases were found deep within the parenchyma of the right lower lobe, measuring 5 mm. and 1.5 cm. in diameter. In the left lower lobe a small metastasis, 3 mm. in size, was found adjacent to a bronchus deep within the lung. These tumors were firm, pearly gray, with a whorled, fibrillar appearance on cut surface and many brilliant zones of necrosis. In the left pleural cavity in the midscapular line, a mass measuring 5 cm. was situated beneath the pleura overlying and incorporating the 6th rib and 5th and 6th intercostal spaces. Its gross appearance resembled the tumor in the neck and spinal cord. No other significant findings referable to this tumor were found in the rest of the complete autopsy.

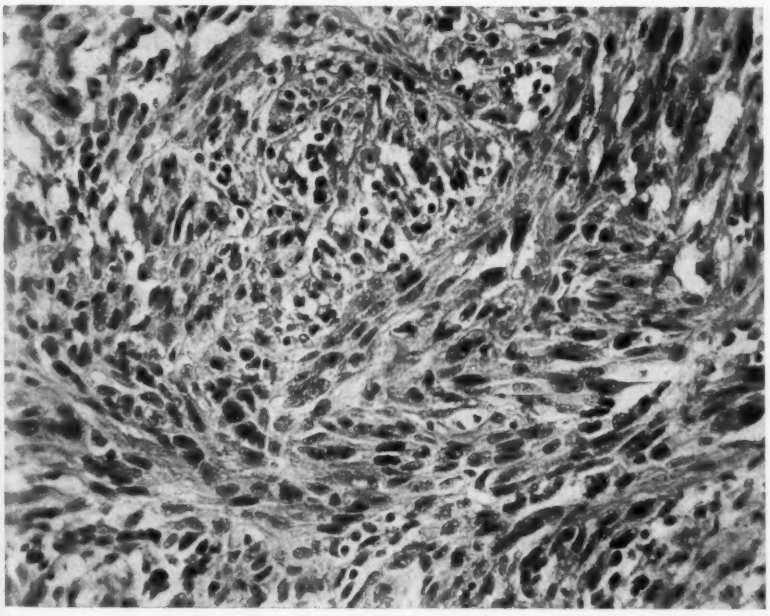

FIG. 4. High-power view of one of the tumor masses in the cervical spinal cord, showing anaplastic spindle-cell sarcoma. (×220)

Microscopic Examination. The tumor cells were elongated and grouped in small bands. The nuclei were round and extremely variable in size and depth of staining, and the cytoplasm was eosinophilic, poorly defined and poorly preserved. Mitotic figures were more numerous, as were tumor giant cells. Collections of lymphocytes were scattered through the tumor. Within the tumor there were indiscrete, round masses suggestive of large nerves. Some of these were composed of dense, cellular tumor, but in others empty spaces suggested empty nerve sheaths, and round, eosinophilic masses suggested swollen axis-cylinders (Figs. 3 and 4). In the adjacent invaded skeletal muscle, nerve trunks were definitely identified. The tumor grew within the nerve sheath and usually invaded the actual nerve itself. The nerves were poorly preserved. *Diagnosis:* This tumor probably represents a neurofibrosarcoma which would be synonymous (according to Stout) with malignant schwannoma.[9]

DISCUSSION

Lanford and Cohn[3] reported a case of ependymal neoplasm of the median nerve occurring on the inner aspect of the right arm. It was thought to be a neuroma and was resected. Seven months later the tumor had recurred in the same region and the arm was amputated below the proximal third. No recurrence was noted 1 year later. Diagnosis: ependymal neoplasm of the median nerve. Stout[4] reported a tumor of the ulnar nerve, and Stout and Murray[8] described a neuroepithelioma of the radial nerve. Cuneo and Rand[1] in 1952 reported a case of malignant schwannoma originating in the distal portion of the left mandibular nerve, and subsequently spreading into the gasserian ganglion and posterior fossa. In reviewing 137 fibrosarcomas and malignant neurofibromas in 100 patients, Stout[6] described these tumors as growing most commonly in the tissues of the flexor surfaces of the extremities and neck, the sciatic nerve being most commonly involved. In addition, these tumors may occur in the upper mediastinum, scalp, intercostal nerves, retroperitoneal plexus, mesenteric plexus of the stomach, duodenum, small intestine and mesentery. Tumors were found arising in the dental nerve, nasal cavity, antrum, lungs, breasts and sacral regions. He described two classes of primary malignant tumors developing in the peripheral nerves—those of mesoblastic origin and those derived from neuroepithelium. The mesoblastic tumors form by far the largest group and may be divided into the uncommon malignant neurofibroma and the common fibrosarcoma. The neuroepithelial group is very small. Tumors derived from ganglia that happen to be situated in various nerves, such as the paraganglioma of the ganglion nodosum situated in the vagus nerve, are not considered primary nerve tumors.

Mention should be made of tumors of the nerve sheath. These occur outside the cranium and spinal canal and are also found within, attached to nerves of various sizes. They cause few symptoms other than the presence of the mass. Stout[5] in 1935 reported 50 new cases and reviewed 194 published cases in a study of the peripheral manifestations of neurilemmomas. He stated that intracapsular degeneration is common and permits transillumination. These tumors have not been found in every part of the body, but in definite localities. They have never been found in the feet, genito-urinary system, lungs, esophagus, rectum, etc. They grow slowly and are entirely benign.

Stout[7] described malignant schwannoma as follows:

"This is a malignant tumor of peripheral nerves derived from Schwann cells. It is not associated with benign neurilemoma but may be associated with neurofibromatosis. About half of the malignant Schwannomas arise in individuals with von Recklinghausen's disease. Hosoi[2] estimates that 13 per cent of the cases of von Recklinghausen's disease develop malignant tumors. This figure is probably much too high. . . . Many mild cases of multiple neurofibromatosis are unrecorded and indeed unrecognized.

"The malignant Schwannoma may occur at any age but is more common in the later years of life. It rarely causes local symptoms other than those due to its mass. Occasionally, when a large nerve is involved, there are symptoms of pain and paresthesia due to pressure upon the nerve or to interruption of its fibers. It infiltrates insidiously, metastasizes freely through the blood stream but rarely through lymphatics, and is frequently fatal.

"Grossly it may produce a fusiform enlargement of a recognized nerve trunk or it may develop from tiny, unrecognized nerve twigs. In this case, the tumor has no specific gross characteristics.

"In vivo and in vitro, like Schwann cells, the cells of malignant neurilemoma grow in cords with the nuclei in tandem formation and tending to palisade. . . . Malignant Schwannomas do not always retain clearly defined histological characteristics, especially in the late stages when metastasis has occurred. Yet, it is unsafe to classify a tumor as a malignant Schwannoma unless some identifying features can be recognized. . . . Just because a nerve is found disappearing into a tumor mass is, in itself, no proof that the tumor arose from that nerve. There are many soft-part sarcomas which by progressive infiltrative growth surround and engulf nerves which they happen to encounter. . . . It is better to call tumors that have only the characteristics of fibrosarcomas by that name and abandon the debatable term "neurogenic sarcoma."

"Various metaplastic tissues are occasionally found associated with Schwannian cells in these tumors."

He depicted the presence of cartilage and osteoid tissue in a malignant schwannoma of the brachial plexus, and stated that rhabdomyoblasts and fat have also been reported.

SUMMARY AND CONCLUSION

Stout opposes the term neurogenic sarcoma because the word sarcoma suggests a mesodermal origin for these neoplasms which are almost certainly neurectodermal and which may better be designated as malignant schwannomas.

The case reported herein is of a malignant schwannoma which originated as an inflamed, dark mole near the right elbow, followed over a period of 6 years by successive recurrences of subcutaneous nodules at the same site. The recurrences progressed higher and higher and finally necessitated amputation of the right upper extremity and shoulder girdle. The tumor finally, extending by way of the brachial plexus, completely invaded the lower cervical cord, causing progressive paraplegia and death. The only sites of metastases found at autopsy were in the lungs and one rib. Apparently the only rational treatment of such a malignant lesion consists of its early and accurate recognition followed by extensive radical surgery and amputation, if at all possible.

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NOTICES

THE HARVEY CUSHING SOCIETY TRAVELING FELLOWSHIP–1957 CONTEST

1. The contest is restricted to residents in training and to neurosurgeons who have entered practice no longer than two years. The essayists must be residents of the American Continent, British Dominions or Western Europe.
2. Two awards are offered: The first consists of a $1200.00 cash prize, the second of $800.00.
3. Successful candidates for these awards will use these funds solely for the furtherance of their neurosurgical education through the means of appropriate travel experience.
4. All essayists will provide assurance that additional funds for traveling expenses, if required, will be available to them.
5. The subject matter of the essay must be the result of personal original clinical or experimental research in neurosurgery or directly related matters. Papers that have been published even in part will not be accepted.
6. Essays will be accepted that are 5000 words in length but not longer.
7. All essays shall be submitted in duplicate to the Editor, the Journal of Neurosurgery, 333 Cedar Street, New Haven 11, Connecticut, U.S.A. with no indication of the writer's name or possible institutional affiliation and accompanied by a sealed envelope containing the contestant's name, address, institutional affiliation if any, details of professional training and a letter of reference from a senior neurosurgeon of the writer's country.
8. Manuscripts will not be accepted after March 1, 1958. They should be sent by registered mail.
9. The Award Committee will be composed of the members of the Editorial Board of the Journal of Neurosurgery.
10. The right is reserved to reject all essays, to withhold or omit awards at any time and to publish the winning essays in the *Journal of Neurosurgery*.

MEETINGS

AMERICAN ACADEMY OF NEUROLOGICAL SURGERY, The Cloister, Sea Island, Georgia, November 11-13 1957. Eben Alexander, Jr., Bowman Gray School of Medicine, Winston-Salem, N. C., Secretary.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE, Hotel Roosevelt, New York, N. Y., December 13–14, 1957. Rollo J. Masselink, 710 West 168th St., New York 32, N. Y., Secretary.

FIRST INTERNATIONAL CONGRESS OF NEUROSURGERY, Brussels, Belgium, July 21–28, 1957. Dr. Marcel David, Hospital Ste. Anne, Paris, Secretary-General, and Dr. William B. Scoville, 85 Jefferson St., Hartford, Conn., Assistant Secretary-General.

HARVEY CUSHING SOCIETY, Statler Hotel, Detroit, Mich., April 25-27, 1957. Dr. David L. Reeves, 316 West Junipero St., Santa Barbara, Calif., Secretary.

LATIN-AMERICAN CONGRESS OF NEUROSURGERY, University of Antioquia, Medellín, Colombia, July 8–11, 1957. Dr. Ernesto Bustamante, Facultad de Medicina, Medellín, Colombia, Secretary.

NEUROSURGICAL SOCIETY OF AMERICA, Key Biscayne, Florida, January 15–18, 1958. Dr. Frank P. Smith, 260 Crittenden Blvd., Rochester 20, N. Y., Secretary.

SOCIETY OF BRITISH NEUROLOGICAL SURGEONS, Royal College of Physicians of Ireland, Dublin, Ireland, May 16–18, 1957 (in conjunction with the Irish Ophthalmiological Society). Mr. D. W. C. Northfield, London Hospital, London E.1, England, Secretary.

SOCIETY OF NEUROLOGICAL SURGEONS, St. Louis, Mo., May 17–18, 1957. Dr. Bronson S. Ray, 525 East 68th St., New York 21, N. Y., Secretary.

SOUTHERN NEUROSURGICAL SOCIETY, Nashville, Tenn., March 15–16, 1957. Dr. C. D. Hawkes, 22 N. Manassas St., Memphis 5, Tenn., Secretary.

SEIZURES FOLLOWING SURGICAL TREATMENT OF INTRACRANIAL ABSCESSES

A CLINICAL AND ELECTROENCEPHALOGRAPHIC STUDY*

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UNTIL recent years the attention of those concerned with the management of intracranial abscesses has been largely directed to a study of the findings in mortal cases.[1,2,5,8,9,12,15,17,18,20,24,26,27,30,32,33,41,51,53,54,60] But now that antibiotic therapy and improved surgical techniques can reduce the risk of death from this dread disease from over 70 per cent to about 25 per cent[1,4,6,7,17–19,24,27,28,31–33,41,42,49,52,54,57,60,66] the morbid—rather than the mortal—consequences of cerebral abscess formation assume increasing importance.

Among these consequences, the three principal disorders that may mar the life of a patient surviving after treatment of a cerebral abscess[8,18,60] are pareses, mental disorders and seizures† (Table 1). These disorders, in the series of cases reported in this communication, occur respectively in 25 per cent, 25 per cent and 47 per cent of the cases of successfully treated brain abscesses. Of all the complications of survival, seizures are therefore the more common, occurring sooner or later in almost half of the patients surviving after treatment of an intracerebral abscess.

Our object, then, in this communication is to arouse interest in the clinical and pathological problems of post-abscess seizures, which form the most important complication of what otherwise may be satisfactory recovery from the disease. For it seems to us that if the principal provocative factors in this connection can be identified, an attempt might be made to eradicate or alleviate them in the course of surgical treatment.

CLINICAL MATERIAL

The clinical material forming the basis of this study is drawn from a series of 100 consecutive cases of intracranial abscess treated, during the past 8 years, in the Neurosurgical Centre of the South-East Metropolitan Region. Twenty-three of these patients had abscesses confined to the cerebellum, and are not considered further here, as none of the survivors had

* A preliminary report of these findings was presented at the Second International Congress of Neuropathology, London, September 1955.

† In this communication the term *seizure* embraces not only muscular convulsions (whether focal or generalised) but also all paroxysmal disorders of sensory and psychical function constituting "sensory seizures" and "psychical seizures."